A B C D E

Med Trib 12

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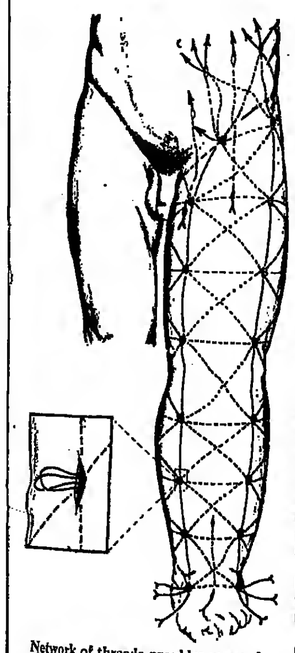
world news of medicine and its practice—fast, accurate, complete

Wednesday, March 27, 1974

Lymph Drainage by Threads



Network of threads provides means for lymph drainage into retroperitoneal space or subcutaneous tissue of the abdomen.

Hepatitis-B Transmitted By Child Bite

By Donald Day
Medical Tribune Staff

San Diego, Calif.—The bite of a 14-year-old retsrdate has been traced as the mode of transmission of hepatitis-B aotigen (HBAg) to a 52-year-old teacher at the child's training school here.

It is not known by what route the HBAg found its way to the retarded boy's saliva. The incident has raised questions as well about the role of HBAg-containing saliva in the transmission of hepatitis-B amoog spouses by mouth-to-mouth contact.

Documenting this case took a good bit of epidemiologic detective work that was helped along with a little blind luck, Dr. Michael MacQuarrie told Medical Tribune.

Dr. MacQuarrie, an epidemiologic intelligence service office of the Center for Diseaso Control (Atlanta) who is assigned to the California State Department of Health in Berkeley, did the investigative work.

The teacher reported symptoms—including nausea, dark urine, jnundice, weakness, and poor appetite—four nnd n half months nfter she was bitten.

It was known at the time of the bite that the boy was an HBAg carrier, Dr. MacQuarrie said, but it was not known then that the disease could be transmitted in this fashion.

The bite was an accident, he added. The boy was choking on some food,

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Nylon Network Used to Drain Lymphedema

Medical Tribune World Service
From German Edition

Wiesbaden, West Germany—A new technique for the treatment of lymphedema of the lower extremities provides drainage of the superficial lymphatics by a network of nylon threads. Dr. Mario Degni of São Paulo, Brazil, the developer, reported here that in 14 patients he has obtained results as good as those of lymphatic-venous anastomosis.

The method of lymph drainage with the nylon network is based on the capillarity along the inserted threads and the pressure gradient between the network and the enclosed tissue during muscle contraction.

By a procedure that Dr. Degni characterizes as complicated to describe but

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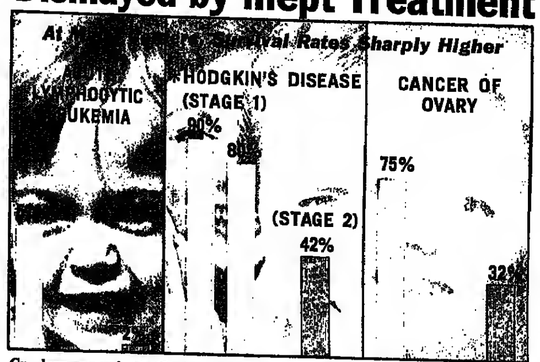
Leading Cancer Specialists Dismayed by Inept Treatment



Gr. bars approximate the improvement in five-year-aliva and cancer-free survival rates in some leading cancer centers queried by Medical Tribune. (See story below.) The earlier survival rates for these forms of cancer are shown in black. Asterisk indicates a 10-year rather than five-year survival rate.

By Ken Sandler
Medical Tribune Staff

Washington—Leading cancer specialists around the nation are becoming increasingly dismayed and discouraged because they feel there are many thousands of unnecessary deaths each year resulting from inept treatment of cancer patients by physicians and hospitals with no business treating such cases.

Some specialists are so convinced that there is nothing they can do within the medical community to enlighten uninformed physicians—particularly general practitioners, surgeons, gynecologists, and pediatricians—that the latest combination chemotherapy and radiation procedures are resulting in astonishingly high *cure* rates that they are ready to take their case to the mass-circulation lay press, such as *Reader's Digest* and the monthly women's magazines, in hope of prompting the public to challenge physicians for proper treatment and for referral to the specialized cancer centers.

Many of these apparently not-widely-known advances in cancer treatment have been in combating "fast-growing cancers," particularly those forms of the disease affecting the young.

At some of the major cancer centers bona fide five-year cancer-free survival rates of 51 per cent have been obtained in the treatment of childhood acute lymphocytic leukemia. Federal estimates sre that 10 years ago the survival rate was 2 per cent. A 10-year survival rate of 90 per cent has been achieved in Hodgkin's disease,

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IN THIS ISSUE

Outpatient Tubal Ligations Save Time, Beds, Costs

Medical Tribune World Service

MONTREAL—When the specialist is well trained in vaginal surgery, a good deal of time, beds, facilities, and their costs can be saved by doing tubal ligations on an outpatient basis, a London, Ont., physician reports.

Dr. Hugh Allen, who heads the department of obstetrics and gynecology at Victoria Hospital, also believes that this tubal ligation procedure is often safer than the laparoscopy technique.

Dr. Allen reported to the Royal College of Physicians and Surgeons of Canada on 700 outpatient ligations carried out using local anesthesia with neuroleptanalgesia. There were 660 partial salpingectomies and 40 Pomeroy procedures.

Some hospital admissions did occur—in 2.2 per cent of tubal ligation cases and in 4 per cent of tubal ligations with therapeutic abortion. However, readmissions were very few.

"In 500 cases of tubal ligation alone, we had six cases of fever readmitted," Dr. Allen told a press conference. "In 200 cases of therapeutic abortion plus tubal ligation, we had one fever case readmitted."

Patient age ranged from 21 to 47 years.

"Close to 90 per cent of these patients were at home in less than eight hours."

In the woman under 30, he advises that "the door be left open." Cutting is recommended in such a way that a repair can be made at a later date.

So far in his repair cases no pregnancies have occurred, but he believes that at present there are three to four possibilities.

Coauthors were Dr. Ralph I. Anderson and John West.

Heart Resuscitator at Cardiologists' Meeting

The safest place for a heart attack was where the cardiologists were—at the 25th annual meeting of the American College of Cardiology in New York—with a fully equipped cardiac resuscitation unit only seconds away. Brain child of cardiologist William J. Grace, college trustee and medical director of St. Vincent's Hospital and Medical Center, the mini-CCU was set up in a corner of the main meeting room. Just outside, a large sign said, "Emergency Resuscitation Equipment Here."

Japan's Infant Deaths Cut

Medical Tribune World Service

TOKYO—Japan claims phenomenal success in reducing her infant mortality in the last half century. The rate, which was running at about 160 per 1,000 live births in 1925, is reported to have fallen below 100 by 1940, and below 40 by 1955. In 1960 the rate is said to have dropped to 30.7, to 1970 to 13.1, and, according to provisional figures of the Ministry of Health and Welfare, in 1973 to 11.7.

Correction

In our story on St. Christopher's Hospice (MEDICAL TRIBUNE, January 23) the correct dosage of injected diamorphine for severe pain should have read four-hourly, not hourly.

Omission

The photograph of a Chinese woman showing her right foot replanted to her left leg (MEDICAL TRIBUNE, February 6) should have carried the credit line: *Courtesy of Dr. Frederick Kao, the American Journal of Chinese Medicine.*

Analgesics Proving Safer With Phenacetin Removed

Medical Tribune World Service

BRISBANE, AUSTRALIA—The removal of phenacetin from most analgesic compounds has resulted in a decline in the number of deaths from acute papillary necrosis in this city, according to Dr. Alastair Burry, of the Royal Brisbane Hospital.

The incidence of acute papillary necrosis is higher in Australia than anywhere else in the world, possibly because of a high consumption of analgesic compounds coupled with a habit pattern of relatively low daily fluid intake and climatic conditions favoring aonurlary fluid loss.

Phenacetin is still used in some of the less popular analgesics but was taken off the Australian Government's list of free drugs in 1967.

Chinese Physicians Flock to Hong Kong

Medical Tribune World Service

HONG KONG—During the past year more than 500 Chinese physicians have flocked here from the Republic.

Most of them were so-called overseas Chinese who left Indonesia, Malaysia, Thailand, and other Asian countries years ago to settle in China and who were educated there.

China now allows them to leave, and many are searching for employment abroad. But bearing only Chinese exit permits and transit visas to their old countries, which do not want them back, they are trapped in Hong Kong. Many have taken menial jobs, and others are unemployed.

Educated Western-Style

According to a survey by the Chinese Medical Graduates Association, most of them have had a five-to-six-year Western-style medical course and have been in practice in China for 10 to 20 years.

It is clear that private practice in Hong Kong has no room for them.

"We already have more doctors than we need," said one general practitioner. "Some doctors I know who practice Western-style medicine find they have to set up two or three different offices around the city to get enough patients."

Many of the refugees are preparing for the examination of the Educational Council for Foreign Medical Graduates to be held in July, in the hope of qualifying to practice in the United States.

'Hats' Knock Sex Lives of Finches Cuckoo

Medical Tribune World Service

ERLING-ANDECHS, WEST GERMANY—The wearing of a hat has a disastrous effect on sexual activity.

In birds, at least.

Anyway, finches.

Eberhard Gwinner, of the Max-Planck Institute for the Physiology of Behavior in Erling-Andechs, Bavaria, arrived at this conclusion in studying the annual cycle of finches and starlings.

Alongside its "internal calendar" which automatically reminds each of these creatures of important and "fixed periods" in its existence, external indicators, such as the number of hours of daylight, also determine the course of the cycle.

Glands Become Microscopic

In winter the genital glands of birds are microscopic. In starlings, the testes weigh only 5 mg. As the hours of daylight increase in the spring, the genital glands also develop—for starlings their weight is up to 200 times that recorded for the winter season.

In normal circumstances the birds' "internal calendar" is synchronized with the astronomical one. It appears, however, that the hours of daylight are not recorded by the birds' visual sense as such but by a light-sensitive organ inside their brain, a "third eye."

Dr. Gwinner proved this experimentally, by separating birds of the finch family into two groups. The study group received caps of black collodion, while the controls wore colorless coverings, through which light was able to pass.

The birds with the black caps could not be stimulated sexually in spite of a 16-hour period of light daily, whereas among the control birds, subjected to the same amount of light, the sexual glands increased in size after only a few days and the creatures showed greater readiness for mating.

The opaque head covering also knocked the birds' migratory timetable into a cocked hat. As the "laboratory spring" proceeded, the controls became more and more restless each day, but the activity indicator among the finches in black caps registered practically no migratory fever.

The necessary information for the synchronization of their annual cycle, then, cannot be due to their sense of sight, said Dr. Gwinner, but where is the point in their brain that is sensitive to light? Among animals of the lower orders—for example, lizards—the pineal gland may be the sensor. For birds, experiments are being done lower down in the hypothalamus.

In future studies, behavioral physiologists want to puncture the black cap in several places in an effort to determine the site of the receptor for sensitivity to light.

Ileostomy Improved Upon

Medical Tribune World Service

STOCKHOLM—Continent ileostomy relieves many of the mental, social, and sexual problems associated with conventional ileostomy, according to the originator of the new technique, Dr. Nils Kock, of Sahlgrenska Hospital, Göteborg.

Dr. Kock constructs within the abdomen an intestinal pouch fitted with a valve that prevents involuntary fecal flow through an opening in the abdominal wall. The patient may empty the pouch several times a day at his convenience, by inserting a tube through the valve.

FDA Makes Big Concessions On Oral-Antidiabetic Labeling

By NATHAN HORWITZ

Medical Tribune Staff

WASHINGTON—Coming down the home stretch in one of medicine's stormiest recent controversies, the Food and Drug Administration has proposed its latest version of the labeling for oral antidiabetic drugs.

The proposed label, reflecting a major FDA retreat from an earlier stand, drops the disputed statement that oral hypoglycemics should be used "only" if diet fails and insulin cannot be employed. The label also omits a lengthy section, "Special Warning on Cardiovascular Mortality," based on the controversial report by the University Group Diabetes Program (U.G.D.P.).

The new version, which still does not altogether satisfy the critics, carries a hold-faced statement, under "indications," urging physicians to consider use of the oral agent in light of "the information" that it "may be associated" with an increased risk of cardiovascular mortality. The label also includes a brief description of the U.G.D.P. findings.

No Indication of Controversy

"The FDA has moved a great distance, but what is missing is an indication of the fact that there is a controversy in this area," said Neil Chayet of Boston, attorney for the Committee for Care of the Diabetic, the nationwide group of experts who organized the scientific opposition to the U.G.D.P. Committee chairman is Dr. Robert Bradley, medical director of Joslin Clinic, Boston.

"The key point that we'd like to see included in the labeling," Mr. Chayet said, "is not only that there is a controversy related to the use of certain hypoglycemic agents but that the U.G.D.P. study itself is the object of controversy. We would want to see the labeling mention that other important studies fail to support the U.G.D.P. findings."

At the FDA, Dr. J. Richard Crout, director of the Bureau of Drugs, stressed that the new labels are not final but are "proposed package inserts which, after modification based on [comments now being solicited], will be published in the *Federal Register* for an additional round of written and oral comment."

Publication in the *Federal Register* is usually the second-to-last step before final promulgation of labeling.

Label to Cite Findings

Mr. Chayet told MEDICAL TRIBUNE that the labeling proposed by the Committee for Care of the Diabetic would mention the U.G.D.P. findings and add: "There is a difference of opinion, among experts qualified by scientific training and experience, as to whether the results of the U.G.D.P. study are applicable in the treatment of diabetes. . . . Other long-term, prospective studies, in which patients were randomly assigned oral hypoglycemic treatment (tolbutamide or phenformin) or placebo, showed no difference in the incidence of cardiovascular mortality or complications.

"In light of the above, the choice of a treatment regimen for the individual patient must be based upon the informed judgment of the physician after consideration of these reports."

At issue in the four-year controversy, which has divided the medical and scientific community almost straight down the middle, are two questions. The first is the validity of the U.G.D.P. findings; the second is the FDA's insistence on revising its labeling on oral antidiabetics in the light of these findings, at a time when they were being challenged by a significant portion of the medical community.

The U.G.D.P.'s critics initially aimed their fire at the study's methods of patient selection and patient management, as well as the statistical techniques applied to analysis of the data. When the study's alleged defects were added up, said the critics, there was simply no basis for the U.G.D.P. finding of an increased cardiovascular death rate among patients on oral therapy. Among the opponents of the study were such men as Drs. Bradley; Rachmiel Levine; Henry Dolger, Professor of Clinical Medicine at Mount Sinai School of Medicine; Peter H. Forsham, Professor of Medicine, University of California, San Francisco; and Holbrooke S. Seltzer, Professor of Internal Medicine, University of Texas Southwest Medical School, Dallas.

The critics' stand was strengthened when the regulatory agencies of Great Britain, West Germany, Sweden, and Canada also rejected the U.G.D.P. findings as "inconclusive" or "invalid."

The dispute, however, moved to a larger arena in 1972 when the FDA issued its proposed new labeling based on the U.G.D.P. study. Angrily, the critics charged that the FDA had neither the moral nor legal right to take sides in an ongoing valid scientific dispute and warned that the agency's action posed the threat of a "government line" in science.

Petition Believed Unique

In an unprecedented step, the Committee for Care of the Diabetic formally petitioned the agency to rescind its controversial ruling (MEDICAL TRIBUNE, November 20, 1971). Use of the petitionary instrument to challenge a Federal regulatory ruling is believed to be unique in the history of American medicine. The 29-page petition and a sheaf of supporting documents charged that the FDA had failed to maintain its mandated policy of "fair balance" and called on the agency to make it clear in its labeling, if it insisted on changing the labeling, that a controversy existed, that the issues were unresolved, and that experts of equal competence took opposing views.

When this move failed, the committee took the case to court and blocked the FDA's proposed labeling changes for two years. The FDA won the court case, but the latest labeling proposed here suggests that the U.G.D.P. critics have moved several steps closer toward gaining the argument.

Sailors Give Aid Abroad

Medical Tribune World Service

ATHENS—U.S. sailors from the aircraft carriers Franklin D. Roosevelt and Independence recently donated 820 units of blood for Greek children with thalassemia.

Stress Snapback May Portend Breakdown

By JONATHAN KAPLAN

Medical Tribune Staff

NEW YORK—A preliminary study gives strong, though tentative, support to the theory that rapid recovery by the autonomic nervous system following mild stress is a sign that may be predictive of a child's later developing serious mental illness—without additional screening for hereditary or environmental factors.

The report was given here by Dr. Fini Schulsinger, the Danish investigator who in 1967, along with Sarnoff Mednick, Ph.D., in a study of children of schizophrenic mothers, first discovered evidence that a rapid autonomic nervous system recovery from disturbance appeared to be characteristic of subjects who were later to suffer a mental breakdown.

In an earlier address before the New York State District Branches of the American Psychiatric Association, in December, 1973, Dr. Mednick hypothesized that the schizophrenic has a peculiar ability to cut off stress or fear stimuli because of his quicker than normal autonomic nervous system recovery. Because of the schizophrenic's "aptitude to reduce fear stimuli," he said, the schizophrenic readily habituates to idiosyncratic patterns of withdrawal from reality.

Study Aimed at Prevention

Now Dr. Schulsinger, working with Dr. Mednick and other investigators, is attempting to utilize the characteristic fast autonomic nervous system recovery in "one of the most ambitious psychiatric studies ever planned." The study is aimed ultimately "at nothing less than the primary prevention of serious mental illness," Dr. Schulsinger told a meeting of the New York State Association of Child Psychiatry.

The study will ultimately monitor 1,800 three-year-old children selected from the general population on the

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ECTOPIC BEAT

From our United Press International wire service: "Escanaba, Mich.—A 17-year-old high school student said Monday he successfully performed a Caesarian section on his pet swordfish."

Obstetricians, ichthyologists, and observers of the passing scene, please note.

(Regular beat: Immateria Medica, page 39.)

news index

CLINICAL NEWS NOTE: *"Well over half the patients in this country with Hodgkin's disease are not getting the optimal therapy." (Dr. Vincent J. DeVita; see page 1.)*

FEATURE INDEX

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IN CONSULTATION

What's new and important in urinary tract infections in children?

The Consultant

DR. JOHN LIBERTINO
Department of Pediatric and Adult Urology, Lahey Clinic Foundation, Boston, Mass.

". . . children do not present with straightforward urinary complaints."

THE URINARY TRACT accounts for about 35-40 per cent of the surgical abnormalities in childhood, so that pediatric urology has become a subspecialty within the broader field of urology. Recent advances in pediatric urology have been made in the management of cryptorchism, exstrophy of the bladder, ambiguous genitalia, vesicoureteral reflux, the megaureter, renovascular hypertension, renal transplantation, and urinary diversion.

There are few developmental disorders of the urinary tract which do not present with—or develop at some time during their course—a urinary tract infection.

Urinary infection is probably misdiagoosed more frequently than any other common condition in childhood. Many children are treated for urinary infection when they do not have one; in others the condition goes unrecognized because the significance of the symptoms is not appreciated and the urine is not examined as a routine. The reason for difficulty in making the diagnosis of urinary tract infection in children is that they do not present with straightforward urinary complaints. The complaint may be vague abdominal pain, inability to thrive, as well as generalized irritability. The gastrointestinal system, or almost any system, may be suspected as the trouble source. The patient is frequently operated upon for appendicitis or abdominal exploration is performed before thorough investigation of the urinary tract has been considered.

Important clues to the diagnosis, in addition to pyuria, hematuria, enuresis, and disturbances of micturition, are such symptoms as recurrent unexplained fever, chronic weight loss, anemia, persistent nausea and vomiting, abdominal masses, abdominal pain, and spinal cord injury. External coogenital anomalies, such as hypospadias, cryptorchism, imperforate anus, and meningomyelocele, should alert the physician to the possible malfunction of the urinary tract even in the absence of suggestive signs or symptoms.

What is the concept of significant bacteriuria and is bacteriuria worthy of treatment?

Pyuria has long been recognized as unreliable in the diagnosis of urinary tract infection. Kass's classical paper in 1956 developed the concept of significant bacteriuria. A urine culture with a colony count of 100,000 organisms per ml, or more indicates a urinary tract infection, but it must be remembered that it does not distinguish a kidney infection from a bladder infection.

Children who have significant bacteriuria should not only be treated but should be evaluated properly once the possibility of urinary contamination has been excluded.

What is the value and safety of bladder puncture in the diagnosis of urinary tract infection in the very young?

Routinely, urine cultures in children should be obtained with the specially designed adhesive plastic bag. An important shortcoming of this method of urine collection is contamination of urine by extraneous sources, such as the vaginal flora. Urine obtained by bladder puncture is rarely contaminated and is therefore valuable in differentiating contamination from true bacteriuria. This procedure, when performed by an experienced individual, gives accurate results and is accompanied by a less than 2 per cent complication rate. The unexperienced operator working on a moving child may expect infection, hemorrhage, bowel perforation, and a broken needle as possible complications.

What is the importance of bacteriuria in neonates?

The neonate with urinary tract infection does not usually present with bacteriuria or symptoms referrable to the urinary tract. They usually present with fever, sepsis, jaundice, convulsions, and failure to thrive, symptoms that may precede the development of bacteriuria.

External features that may accompany congenital urinary tract anomalies should indicate the infants at risk (e.g., absence of the second artery in

Continued on page 9

If there's good reason to prescribe for psychic tension...

Prompt action is a good reason to consider Valium® (diazepam)

When, for example, despite counseling, tension and anxiety continue to produce distressing somatic symptoms

When your patient's somatic complaints are associated with tension and anxiety and you have tried counseling and other supportive measures alone, you may decide to prescribe psychotherapeutic medication. If you do, the question remains: Which one?

Valium (diazepam) is one to consider closely. One that works promptly as an adjunct to continued supportive measures. One that generally produces significant improvement within the first few days of therapy, although some patients may require more time for a clear-cut response.

Prompt action. One good reason to consider Valium (diazepam).

And should you choose to prescribe Valium, you should also keep this information in mind: Valium is usually well tolerated; the most common side effects reported have been drowsiness, fatigue and ataxia. As with all CNS-acting agents, patients should be cautioned against operating dangerous machinery or driving. Normally, therapy with Valium (diazepam) should be continued until the patient's psychic tension symptoms have been reduced to tolerable levels.

Please turn page for a summary of product information.

Valium® ROCHE
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One Man... and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

Real Crises vs. Red Herrings

I AM REALLY FED UP. We have no need for phony crises. Problems abound. Issues exist. There are enough dilemmas to create plenty of true crises of conscience. We need a willingness to honestly confront issues with a reality of vision and with balanced perspectives.

If we could save the energy expended on imaginary or inflated problems, we would go a good way toward solving the energy crisis. The pity of it is that so many sensible and well-meaning Americans are being either led by the nose or blinded by the slogans of others, some well meaning and some not quite so.

Perspective in Problems

Let's take the ecology bit. MEDICAL TRIBUNE was one of the first publications, scientific or otherwise, to raise the issues of pollution, years before ecology had become a household term. But MEDICAL TRIBUNE has always sought to place this issue in perspective. Even as it sought public recognition and action in the areas of air and water pollution, MEDICAL TRIBUNE always stressed the immediate overriding mortality and morbidity of personal pollution, such as cigarette smoking—deaths alone in the range of a quarter million a year. MEDICAL TRIBUNE pioneered for auto safety and seat belts before many, if not most, of the present-day consumer advocates had even realized the realities of that problem.

The "drug crisis" swept the nation. Since its founding, MEDICAL TRIBUNE pointed the dangers of one of the most dangerous drugs of all and one of the most habituating of substances—alcohol. In the hectic and headlong rush for headlines, our "public statesmen" panicked public and parents alike. The "drug problem" was real enough, but it was and is minuscule from a strict public health point of view when compared to that most dangerous of all addictions—alcohol. Drug problems remain, even as the drug hysteria seems to have ebbed a bit. Many who sought career gains from its exploitation had to confront other issues. An "honest voice," the official report of the National Commission on Marijuana and Dangerous Drugs, collected and published the real facts as they relate to the addiction crisis. The problem was not marijuana—it was and is alcohol.

Crisis Atop Crisis

Then, of course, we have the "overpopulation crisis"—horror or hoax. I do not here raise the issue of the right of an individual to the best contraception technology or personal resort to abortion. I do believe that every thinking person should face the issue honestly and not be stampeded by hysteria consciously created by people with axes to grind. There is enough data on hand to show that birth rates fall when people have good food, good jobs, good education, good housing, and low infant mortality.

We have a health care crisis, and a crisis it is. But can one really gain the measure of the problem from the press, from the public posturings and the political pronunciamentos to which we are exposed? Perhaps it is expecting too much; perhaps one must learn to live with the realization that public figures will always tailor their publicity cloth to fit their political ambitions. We "declare war" on cancer and heart disease—and impound health funds.

Consistent with Reality?

In the face of waiting lists and long waiting times in doctors' offices, in the face of the unavailability of primary care physicians for home calls and for many areas of the country, and particularly for depressed and inner city areas, government officials pronounce the "adequacy" of our health manpower. Of course, such a pronouncement is consistent with impoundment and reduction of health training funds, but totally incousistent with such realities as the staffing of American hospitals.

For example, in 22 Baltimore-area hospitals, of 1,452 physician staff members (interns and residents, etc.), 51 per cent graduated from foreign medical schools, the minority came from U.S. schools. At issue is not the adequacy of the men who came from 69 different countries but rather the shameful situation that the United States, with its enormous backlog of qualified premedical students, is constantly draining highly skilled medical manpower from such impoverished areas as Bangladesh, Cameroon, and Honduras. Only 10 per cent of the Baltimore-area foreign medical graduates came from Europe. This is a disgraceful exploitation of essential resources of poor nations.

America's Unheld Hearings

Or take the issue of health care costs. Even as they were escalating through the ceiling, solemn hearings were held *not* in respect to 60 per cent of the hospital expenses, which were payroll, nor, for that matter, to the 4.5 per cent of the costs for raw food and utilities, but instead to the price of drugs, which currently constitute only 2.8 per cent of total hospital expense. How one can expect to counterbalance an escalating 97.2 per cent of hospital costs by reducing the 2.8 per cent cost of drugs escapes me. What does not escape me is the incredible cost in billions and the untold suffering that would still be the lot of patients with tuberculosis, psychoses, poliomyelitis, osteomyelitis, and other either preventable or treatable conditions if we did not have the medicines now at hand.

Like our medicines, doctors—who, thanks to the good sense of the public, are still rated as the most credible group in our society—are subject to critical attack by many who are rated as the less credible categories of our society. It is a fascinating commentary on our times that Professional Standards Review Organizations have been legislated by Congress and the regulations are now being formulated by the Administration not for lawyers, not for political figures, but for the medical profession. One marvels at that fantasyland called Washington.

Political expediency knows no bounds. The Government proclaims a freeze on hospital costs as part of the health industry and would seek to control charges on a per admission basis. Is this not another phony ploy? How can hospitals meet their escalating fuel costs, the rising cost of living of their employees, yet provide the same services at the same prices as in the past? There are those who would believe there is no limit to public naïveté.

Under the "Crisis" Blanket

Now, of course, we have the "energy crisis." After all the wheel spinning and headline hunting of the "ecology crisis," the "drug crisis," the "overpopulation crisis," I stand in utter amazement and watch us line up like sheep for blocks around gasoline stations. It is astonishing. Petroleum is not just gasoline. It is warmth in the home and food for the family. It fertilizes our fields, runs the tractors, and provides pesticides. It is transportation to our jobs. It is the basis of essential medicines.

While "crisis" after "crisis" was exploited, real shortages and spiraling price increases were taking place under the noses of our "visionary statesmen." Think of the energy expended in not attacking real problems in a realistic perspective but in "heroically" hauling around a batch of red herrings.

William Osler

Through his teaching and personality, Canadian-born William Osler (1849-1919) greatly influenced American medicine. At Johns Hopkins University, he introduced the concept of senior students' actually taking part in the management of patients. His textbook *Principles and Practices of Medicine* (1891) went through eight editions during his lifetime and was translated into four languages.

Canada issued the stamp in 1969 in Dr. Osler's memory.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

IN CONSULTATION

Continued from page 5

the umbilical cord, prune belly syndrome, spina bifida, a single transverse palmar crease, abnormalities of the pinnae [hat ears], and lateral displacement of the nipples). With a high index of suspicion, urinary tract infections in the neonate, although difficult to diagnose, should not be missed.

What is the proper work-up in the diagnosis and treatment of urinary tract infections in children? What are your recommendations in the case of a first infection in a five-year-old (1) girl? (2) boy?

One must first document that this is truly an infection and not contamination. Whether every child should have a full investigation, including IVP, VCUG, pressure studies, and endoscopy, at the time of their first attack is a matter of discussion. The majority of pediatricians and pediatric urologists are in favor of at least obtaining the first two examinations.

I would perform an IVP initially on both children and a VCUG on both children after their acute infection subsided. Because of the high incidence of urethral valves in males, I would endoscope the five-year-old boy and would endoscope the female if she had a subsequent infection.

Next In Consultation

DR. EDWARD F. ROSENBERG, Clinical Assistant Professor of Medicine, Chicago Medical School, University of Health Sciences, Chicago.

. . . will consolidate the rapidly accumulating developments in total joint replacement—"a quiet surgical revolution," he calls it.

Please comment on the significance, role, and management of ureteral reflux.

It is clear that vesicoureteral reflux is a principal cause of pyelonephritis in childhood and that its surgical correction should be considered in some cases but certainly *not all* cases.

Reflux should be surgically corrected in children who have any of the following:

- Recurrent urinary tract infection with breakthrough on proper drug therapy.
- Failure of the kidneys to grow with age.
- Deterioration of the upper tracts radiographically.
- Compromise of renal function.
- Golf hole orifices with low pressure reflux and altered upper tracts.

Proper antibiotic medical management is advocated in children who do not fall into the above categories.

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Phenobarbital

PHENOBARBITAL, which was introduced in 1912 and was marketed under the trade name Lumioal, is the second oldest barbiturate, its predecessor in 1903 having been barbital, or Veronal. Phenobarbital rapidly achieved a reputation both as a sedative and as an anticonvulsant; in the older pharmacy texts and dispensatories, those are the rubrics under which it is principally considered, together with descriptions of problems of toxicology, idiosyncrncy, and habituation.

In the past 10 years or so, however, more interesting charncteristics of the barbiturates in general and of phenobarbital in particular have surfaced. Barbiturates are now known to stimulate the activity of hepatic microsomal enzymes, in addition to possessing other qualities. Thus, as is by now well recognized, phenobarbital increases the rate of metabolism of bishydroxycoumarin and can thus affect the prothrombin time of patients receiving that drug. Phenobarbital also hastens bilirubin's conjugation with glucuronic acid and is therefore prescribed in infants with congenital nonhemolytic jaundice to reduce the serum bilirubin. Porphyrin synthesis is controlled by ALA synthetnse, an enzyme in the mitochondrin of hepatocytes. Since the barbiturates stimulate formation of this enzyme, they are contraindicated in patients with acute, intermittent porphyria.

One of the lesser-known properties has been described as "the tolersnce to the effects of ingested alcoholic beverages exhibited by persons who use barbiturates regularly." In a study performed by Drs. Esteban Mezy sod Enrique A. Robles at the Johns Hopkins University School of Medicine, administratioo of phenobarbitsl 240 mg. daily in divided doses for six dsys was shown four days later to have enhsnced the rate of alcohol disappesrance from the blood of four subjects hy about 20 per cent over hsseliocs. This cnreful study, reported in the February issue of *Gastroenterology*, did not succeed in showing, however, that incrense in the rate of ethanol disappearsnce was due to nay change in the activitics of either alcohol dehydrogenase or of nicotinamide adenine dinucleotide phosphate–dependent microsomal enzyme in homogenates of liver biopsies. Both enzymes catalyze the oxidation of ethanol.

As the nuthors note, other effects of phenobarbital might be responsible. Thus they state, "In animals, phenobarbital has been showo to increase weight and protein content of the liver, hepatic blood flow, and biliary flow." They favor increasen in hepatic blood flow and biliary flow as perhaps having contributed to the rate of ethanol clearance.

In any event, the properties of phenobarbital are diverse aod, to a degree, surprising.

What's in a Name?

THE SEDATIVE-HYPNOTIC DRUGS that comprise the barbiturates are all derivatives of barbituric acid, which is malonylurea. Barbituric acid, which, uninhibited, has no sedative or hypnotic properties, was synthesized by Adolph von Bayer in 1863, when he was 29 years old. Some references say he named the product "in honor of a friend, Fraulein Barbara." Others say that the day he synthesized the compound he visited a tavern that was a gathering place for artillery officers. As it happened, that was the Day of Saint Barbara, the patron saint of artillery officers. Ergo, Bayer joined Barbara to urea to name his compound barbituric acid.

Whatever the exact origin, there is no doubt that a lady's name was involved. A better-annotated use of a lady's name in biomedical nomenclature is attached to the labeling of HeLa cells. Medical dictionaries simply say that HeLa is derived from the name of the patient whose cervical tumor was the source of the cells isolated by Dr. George O. Gey in 1951 to serve since then in a spate of tissue culture techniques. Well, the patient was Henrietta Lacks. As the *Medical Journal of Australia* puts it, she "has achieved test-tube immortality and the gratitude of scientists and patients all over the world."

But the truth of the matter is that the name of origin rapidly vanishes in the mist of time, and all that remains is a generic term devoid of its historic connotations.

Propranolol and Angina

CLINICAL QUOTE: *"Thus, the frequent practice of increasing propranolol dose until the patient is pain free may not be clinically sound since with reversal of the usual angina-fatigue relation, potentially severe myocardial depression may be overlooked despite the fact that pain is absent."* (Dr. William H. Frishman and colleagues, at the Coronary Artery Medicine and Surgery Conference, Houston, Tex.; see page 36.)

"I thought it was a little too realistic for Marcus Welby. Seems we've somehow got hooked into closed circuit at Bellevue."

LETTERS TO TRIBUNE

Scrotal Sag Syndrome

The recent symposium in Philadelphia on "Sexual Problems of the Aged" brings up a particular problem with the male. Dr. Hsrold Lief, in his discussion which appeared in MEDICAL TRIBUNE of Jsnuary 9, gives a very good evaluation and comes closest to helping solve these problems.

However, a little more could be ssid. Although he ascribes the "estrangement snd depression" which occur in this society to the subordination of "the sense of touch to the demsnds of the genitals," I think that our cultural attitude about the genitals is part of the problem. Dr. Eric Pfeiffer, also at the panel, talked about the feeling of embarrassment about less extended performance when the male can't keep his erection and has to go to the doctor to see what's wrong. However, the doctor to whom he may go is probably a man of his own age or older, and he too has the same problem as the patient. The average male who is in his 50s or 60s has been brought up with a concept that sex is dirty, taboo, it has to be hidden. His own attitude makes it difficult to help his patient. He may have, along the way, become more sophisticated, but emotionally he still has the attitudes of his childhood.

When the male gets old, the scrotal sac is the part that sags, just as the breasts of his wife sag. He gets very upset. Dr. Lief comes closest to pointing this out when he says that the male worries sbout his ejaculate, which has begun to diminish. From what I have seen, this is precisely what he worries about but usually denies, as he's been wont to do all his life. True, his ejaculate has diminished markedly, his sac shrivels, and the testes get smaller and atrophic. It is this that worries him perhaps more than whether he can hold his erection a little longer. Obviously the erection is of major importance to males, but the added worry about his ejaculate combines to bring him to the doctor.

I think it would be really helpful to the male if he could get a feeling from his partner that he is loved whether he produces or doesn't. It's past the time for that much producing anyhow, and perhaps if we can educate him, as one always needs to do in these areas, we can give him a better feeling of self-worth, without making the equation that the male so often makes: he equates his intellectual ability with his opinion of his genital. This is an unconscious equation, but it plays havoc with his self-esteem at certain times in his life.

I agree with Dr. Lief that Freud has indeed led us astray with his standards about the only mature sexuality being coital sexuality. Time, new ideas in a changing society, and a freer attitude about sexual activity have shown us that there is a great deal more to be said.

ANITA I. BELL, M.D.
New York, N.Y.

'The Sexy Naked Ape . . . .'

Dr. Sackler, in the issue of February 6 of MEDICAL TRIBUNE, displays nothing on the subject of the population explosion except his profound ignorance of the facts of the situation of mankind.

Let me point out to Dr. Sackler that those organizations which have wrestled with environmental problems for generations have all concluded, along with Zero Population Growth Incorporated, that their goals of a cleaner instead of a dangerously polluted, poisoned environment and the preservation of wilderness are utterly unattainable without stabilizing population. These organizations include the Sierra Club, the Wildlife Federation, the Audubon Society, and the Friends of the Earth. They have all seen that their goals are utterly unattainable if mankind's present growth rate, which is 2 per cent over the earth, is not stopped and brought to zero soon.

The most monstrous, fallacious con-

Continued on page 30

Inept Treatment Dismays Cancer Specialists

Continued from page 1

when diagnosed in stage 1, and 80 per cent in stage 2. Ten years ago, the five-yaar rate was 42 per cent over all. Five-year ratas for cancer of the ovary are reported as high as 75 per cent. Ten yeors sgo, the rate was 32 per cent.

It should be noted that the latest five-year survival ratcs reflect treatment protocols used st least five years ago—and the sophistication of the protocols, particularly in combination chemotherapy treatment (some call it poly-chemotherapy), has aince improved.

Often Not Up to Date

All too often, the dissatisfied specialists believe, private physicians and hospital staffs treating cancer patients are not up to date on the latest protocols, do not see enough patients with a particular form of caocer to develop the expertise required in offering care, take a fatalistic attitude toward the patient, often attempt inadequate therapy, and, after tbe patient detariorates, refer him to a specialty center.

Because tbe protocols have been developed ioch by inch, too many older physicians are unaware of treatmant methods now available, and many are prejudiced against chemotherapy, on which the new protocols are bascd, because of old reports of severe side effects and little beoefit.

Many of tbe new therapies also requlre a team approach that spans the specialties—a treatment method not often available in community bospitals; but bospitals across the country continue to accept cancer patients without being able, through lack of informed, experienced staff, to offer optimal care.

Ona of tbe most vociferous opponents of second-rate treotment is the chief of the Medicina Branch of tbe National Cancer Institute, Dr. Vincent J. DeVita. "I'm furious," he told MEDICAL TRIAUNB. "Physicians condemn new modalities on the basis of previous experience with a few patients. They say, 'I've seen enough people killed with cbemotherapy'—and they decline to use it.

New Tharapy Resisted

"There is a certain amount of resistance in the medical community to naw therapy. The doctors don't read about it, tbey often don't believe it's succesaful, and evco when tbey do read about it, they bave to see it to believa it."

"They look at you and talk about a garbled therapy program tbat a third-year medical student wouldn't use and than say tbat it doesn't work," Dr. DeVita complained.

"It's a problem of medical communications. I ask them, 'Suppose there is a new tberapy for a specific disease. What would it take to convince you to use it?'

"Tha whole bloody thing is this feeling that if you have cancer, it's bopeless. Many times they use the proper therapy—when it's too late. Thus, it's a self-fulfilling prophecy. I've given up trying to convince physicians."

He cited a New Jersey-Delaware-Pennsylvania survey that showed 90 per cent of the reported cases of ovsrian cancer were being privately treated instead of heing referred to cancer centers.

"We've got to convince private gynecologists that there is something you can de other than surgery. The gynecologist is either going to have to share the patient or give her up entirely.

"And even good M.D.s are compromised hy the economics of treatment. Give them an alternative [cheaper] therapy and they will take it," Dr. DeVita said.

At the National Cancer Iostitute "we think you should refer patients to the centers, but M.D.'s question why. Why? Just because a study is being done by the center is good enough reasonl But the doctor says, 'I'm an oncologist. Why should I refer my patient to a ceoter?' "

"We could save thousands. Three thousand out of the 10,000 deaths each year from ovarian tumors, 3,000 to 4,000 deaths from Hodgkin's disease," for example, could be prevented by the latest treatment, Dr. DeVita asserted.

Many Get Suboptimal Tharapy

"Well over half the patients in this couutry with Hodgkin's disease are not getting the optimal therapy.

"But many M.D.s get their backs up every time they hear this—and sometimes then refer fewer patients to tbe centers."

Ha said that soma physiclans believe that "chemotheropy is soved for advance patients, surgery for localized cancer, and radiation therapy for in-between. They're not pulling it all together—and they've go to."

Dr. DeVita emphatically stated that "the only way to make the latest therapies quickly known is to got the information out in the lay press and have patients aay to their doctors, 'Hey, I read about that therapy.' "

When they see a patient with cancer too many physiclans, particularly those wbo do not see many cases, Dr. DeVita cborged, say "I'd rather have the patient dead" than have him go through arduous therapy.

"This kind of information has to be in the hands of tbe public—so they can say, 'I'd like to get another opinion.' "

The Natiooal Cancer Institute has begun to set up a network of treatment demonstratioo centers, with 12 centers now in operation and six more planned, all of which are in leading institutions.

The demonstration-center concept is designed to bring physicians to the centers for education and training io the latest protocols and to persuade tbesa M.D.s that if they lack the skills needed to offer optimal care, they should refer their patients to tha major cancer centers.

Dr. Gerald P. Murpby, director of Roswell Park Memorial Institute in Boffalo, N.Y., told MEDICAL TRIBUNE: "We have got to get ioformation on tbe latest poly-chemotherapies to our medical colleagues, and we've got to do it fast.

"We've been grappling with this problem since 1972, and we feel that the best method is through the cancer demonstration center approach. Tbe center system is the one we cnn most rapidly assemble, and we bave to push this system harder."

Dr. Audrey E. Evans, directnr of oncology at the Children's Hospital in Philadelphia, told MEDICAL TRIAUNE: "For a cancer patient, the institution you're in makes a significant differencc whether you live or die. Ynu don't go to your lucal [community] hospital for cancer carc.

Puts Hopas to Public

"It's terribly important that we spread this information. I've decided to hit the women's mngozine market to make this informotion generally available. If we can get it to the lay public, maybe they would do something.

"The family physician just can't keep up. A remarkable number of doctors don't know of the advances made in curing childbood cancer. They are 10 years behind in their knowledge."

Dr. Evans stated, "We nced o stronger method of getting the information out to the doctors. And we must get the mcssage out to the smaller hospitals."

One of the methods she suggested is the creation of regional tumor regiatries—a system advocated by the American College of Surgeons. By having statistical breakdowns of the numbar of cases of each type of cancer that each hospital treats—and the survival rate at each facility—it would soon become appareot which hospitols are offering the best treotment.

Dr. Evans also called for adoption of the team approach—including chemotherapy specialists, radiologists, and surgeons—in treating cancer and routine open discussion abnut all cancer patients by tho team physicians.

Dr. Joseph Simone, chief of hematology at the St. Jude Children's Research Hospital in Memphis, Tenn., tuld MEDICAL TAIBUNE: "A G.P. will see two cases of leukomin in his lifetime, and he doesn't read abnut advances in treatment in the literature because it's not in the journals he reads . . . ond there are guys who haven't read a journal since 1924 who think they are qualified to treat cancer.

"One thing we could do would be to go into the doctor's office and tell him, but even that might not change every doctor's mind.

"A doctor who accepts the responsibility for the definitive treatment of o child with cancer should be qualified to deliver all facets of care and should take the responsibility for this life-and-death situation. But vast numbers of G.P.s are not qualified, and 99.9 per cent of the pediatricians are nnt qualified," he said.

Dr. Simone lamented about the pediatrician who treats a child for cancer and than, "when he gets into hot water, be punts" to the specialized center when he should have referred the patient initially.

"There are a hell of a lot of physicians on the East and West coasts who, because they spent six months treating cancer patients during their residency, think they're qualified to do anything. But the outlook [and treatment modalities] have changed while they've been in practice" and they are not aware of it.

Dr. Lester Breslow, dean of the U.C.L.A. School of Public Health, told MEDICAL TRIOUNE that "cancer patients ore dying because they did nnt receive the best that is available in Americnn medicine.

"Typically, in an endeavor to improve the standard of health care, a small segment of a profession develops the expertise, then some professional body begins to furmulate standards and promote them. At n certain point, when the public interest justifies it, there is Guvernment licensing."

May Mean Limtting Cara

"It would be very appropriate for the Government to cunsider . . . standards to assure the best quality of cure for cancer patients, and if it means limiting [who can provide the] care, then that's the thing to do," Dr. Breslow suggested.

Addressing the issue of treatment for the less common cuncers—which call for physicians with substantial experience—Dr. Breslow suggested that "people would be much better off if only a few institutions would develop the expertise in trent these rarer cancers" ond then have all such cases referred tn these facilities.

The Americnn College of Surgeons hus o cancer accreditotion program for hnspitals ond has certified about 800 institutions, nn either a full or provisional basis, as having "the appropriate organizotiun, personnel, and facilities."

The requirements for certificatioo include a hospital tuamr registry, a follow-up on cancer patients, and organizatinnal structure.

But the program does not attempt to gauge, nr even imply, any judgment of expertise or the quulity of care available at certified hospitals.

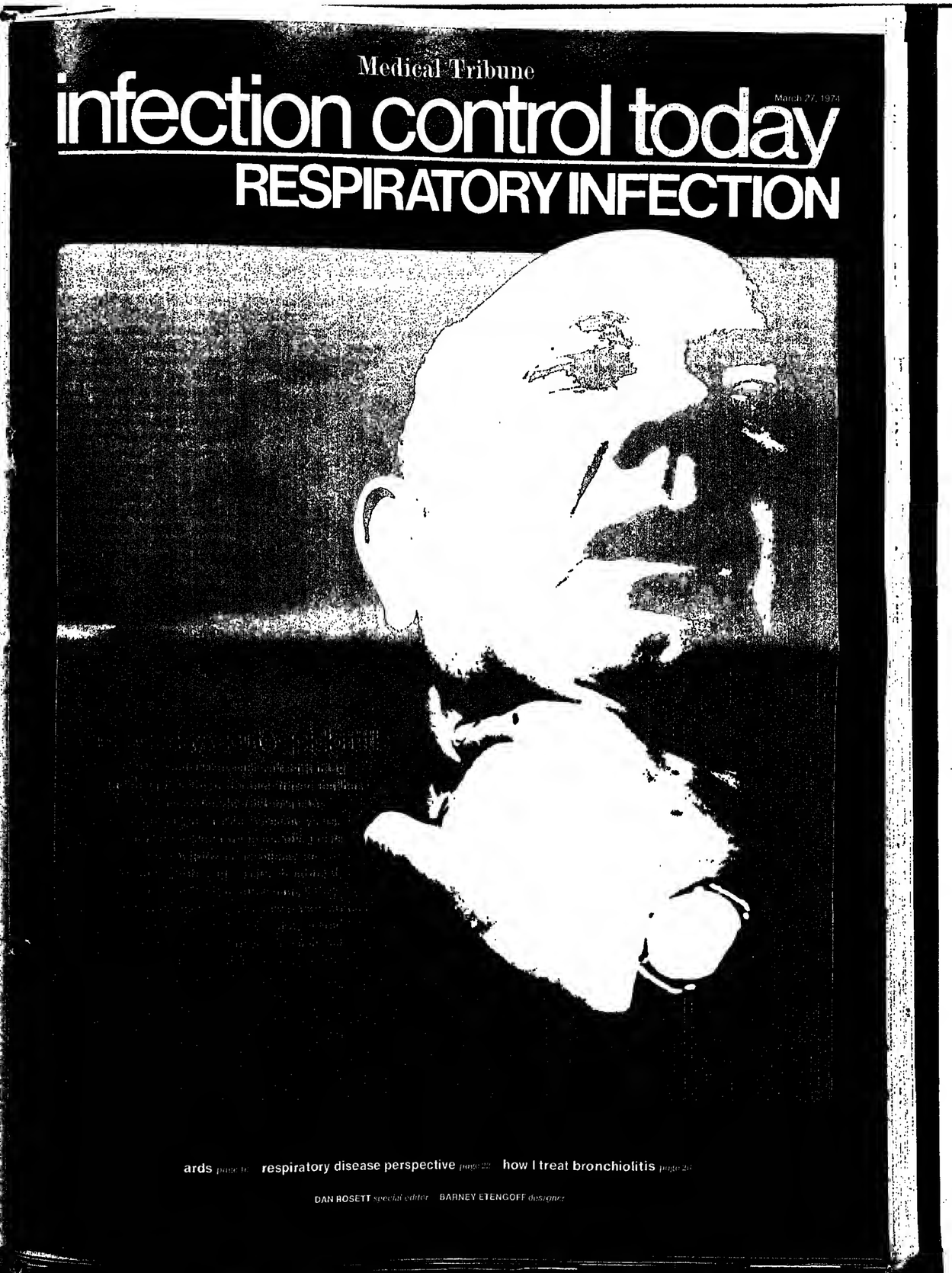
Dr. Andrew Mayer, assistant director nf professional uctivities of the A.C.S., in discussing the cancer treatment situation with MEDICAL TRIBUNE, echoed the belief common to niany surgenns: "Chemotherapy is still in the experimental stage—it prolongs the life of a few people but makes their lives pretty miserable for the few extra months" it gives them.

Instead, he stated, "we're looking to immunotherapy as a major area" for progress.

Cats Aid Tay-Sachs Study

Division of Research Resources Photo

A family of Siamese cats lacking the nctivity of the beta-galactosidase enzyme is being studied by Dr. Henry Baker, of the University of Alabama, for clues to Toy-Sachs disease.



epiglottitis

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tis and subsequent obatruction of the airway. As a result, both diagnosis and treatment remain controversial.

Etiology

In children, Hemophilus influenzae type B is the recognized cause of most, if not all, cases of acute epiglottitis. In adults a variety of bacteria have been reported, including H. influenzae, which causes the most severe and rapid progression of respiratory distress. Pneumococci, beta-hemolytic streptococci, and staphylococci have been cultured from adult epiglottitis, but frequently cultures directly from the epiglottis are not taken and may well be imprecise in defining causative factors.

Recent studies suggest that, because of the frequent use of antibiotics in combating respiratory diseases, some children never develop immunity to H. influenzae and, as a result, meningitis and respiratory infection due to this organism are being noted with increasing frequency in adults.

Dr. Donald B. Hawkins, Assistant Professor of Otolaryngology at the University of Southern California School of Medicine, reports that in the last 10 years 17 adults have been managed for acute epiglottitis at Los Angeles County Hospital, 13 of them within the last four years. Five additional patients were treated during this past year alone.

Symptoms

Suggestive symptoms of epiglottitis in both children and adults are the onset of fever, sore throat, dysphagia, drooling of saliva, and hoarseness or a muffled voice. A gurgling inspiratory stridor and anxious expression are often noticed, and the patient may sit up and lean forward to facilitate breathing.

"There is sometimes difficulty in differentiating epiglottitis from subglottic obstruction," Dr. Hawkins points out. "In the latter case the child will usually have a more pronounced inspiratory stridor with retractions, and when he coughs it is barking and croupy. More severe subglottic laryngotracheobronchitis usually occurs in children under age two, whereas you don't see many cases of epiglottitis under two."

Epiglottic abscesses are an additional complication in adults but not usually in association with H. flu. They may need to be drained to prevent obstruction.

Once epiglottitis is suspected, most physicians are reluctant to make a firm diagnosis and proceed with vigorous treatment without visualizing the epiglottis. Direct visualization, by depressing the tongue, may have catastrophic consequences by precipitating obstruction. Similarly, making the patient lie down to insert a laryngoscope is also unwise, and the inexperienced physician may have difficulty in seeing the epiglottis. For this reason, radiographic examination is often preferred for those to whom the services of an experienced otolaryngologist or aneathesiologist are not available.

"As ear, nose, and throat specialists we can do indirect laryngoscopy very easily in most adults and in some older children, and it's also much easier for us to do direct laryngoscopy," Dr. Hawkins notes. "However, we don't like to do direct laryngoscopy on a child we think has epiglottitis unless we are prepared to establish an airway, either by inserting a bronchoscope or an endotracheal tube right away, because you may get into trouble once you lie the patient down."

X-rays helpful

"This is a big problem for a pediatrician who is not really trained to do laryngeal examinations," he feels, since the pediatrician is at a disadvantage, and for him x-ray diagnosis through a lateral x-ray of the soft neck tissue is sometimes helpful. However, Dr. Hawkins feels there are limits to its usefulness if the child is in acute respiratory distress and warns physicians to be very careful in keeping the child upright all the time lest the patient's airway become obstructed immediately.

This danger of rapid obstruction is the specter that haunts most physicians, who fear they will not have time to establish an emergency airway, since respiratory and cardiac arrest may occur at the same time. For this reason, some feel strongly that the time and distance away from emergency care taken up by radiography is life-endangering and that x-rays have no place in emergency diagnosis.

Given a patient with mild to moderate respiratory distress, x-rays are an infallible way to diagnose epiglottitis, which, "once seen, can never be forgotten because of its striking appearance," according to Dr. James D. Baxter, Professor of Otolaryngology and department chairman at McGill University and otolaryngologist-in-chief at the Royal Victoria Hospital in Montreal.

Difficulty in visualizing epiglottis

Dr. Richard Rapkin, director of pediatrics at Children's Hospital in Newark, N.J., a staunch supporter of radiographic examination, points out the difficulties in visualizing the epiglottis and the frequent mistakes made in diagnosis.

"Among 50 patients studied with evidence of upper airway obstruction, 39 had an admission diagnosis of nonbacterial croup and 11 were admitted with the diagnosis 'rule out epiglottitis.' Three patients from this latter group all proved to have epiglottitis."

"Examination of the pharynx was done in all patients," he says. "Of the 47 patients with nonbacterial croup, the epiglottis was seen poorly or not at all in 33; it was seen well and thought to be normal in 10

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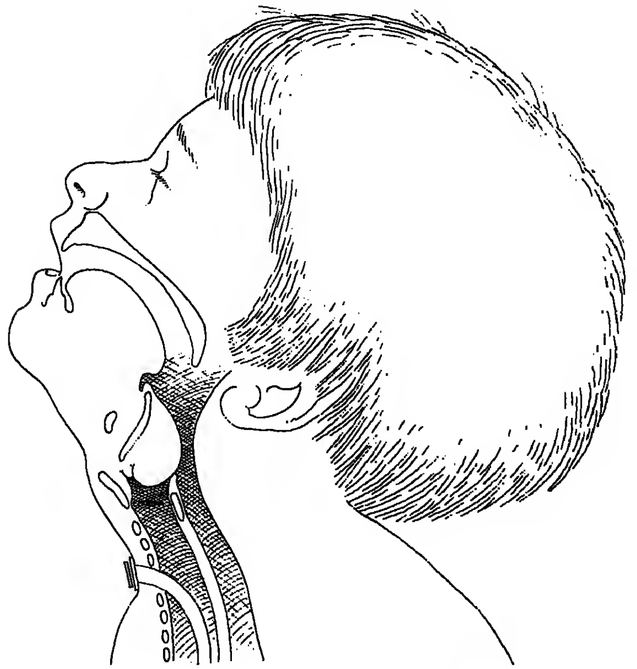


Dr. James D. Baxter

Dr. Donald B. Hawkins

adult respiratory distress syndrome

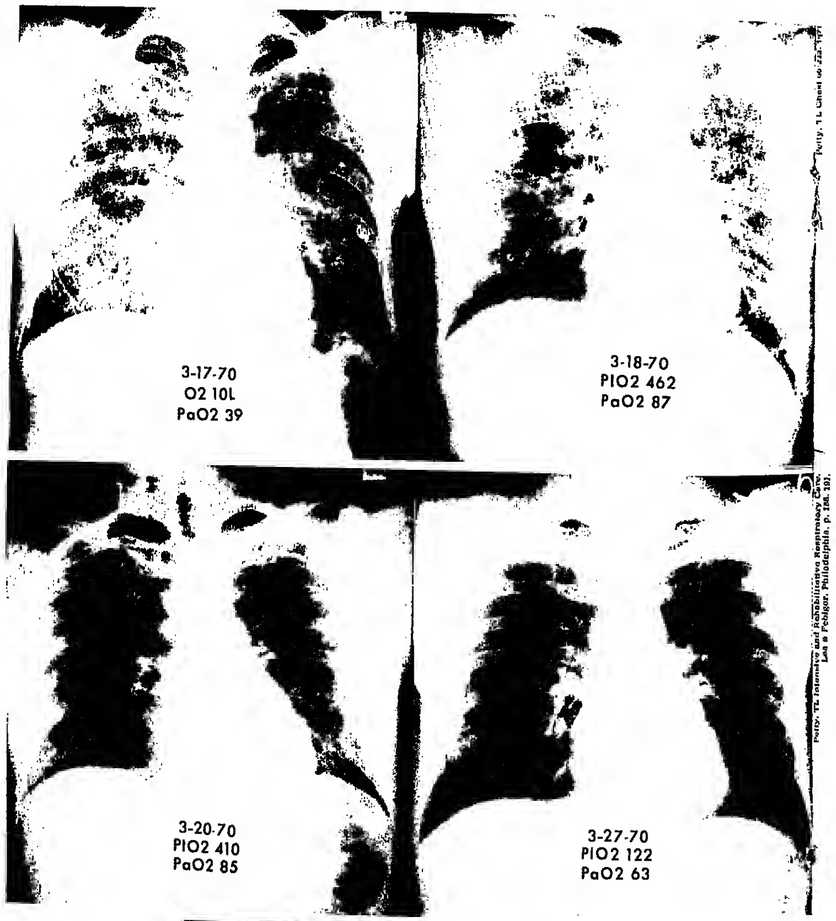
SECONDARY INFECTION is the leading cause of death in patients with the adult respiratory distress syndrome (ARDS), a respiratory emergency not yet clearly understood even by pulmonary specialists but believed to be a nonspecific response to a variety of pulmonary injuries.

Etiology

Chest trauma or the pulmonary effects of shock, viral or aspiration pneumonia, sepsia, or major surgery may trigger acute respiratory insufficiency in adults. Although the pulmonary changes are largely reversible, the outcome often is fatal.

"Fatalities are usually a result of septic complications, including pneumonia, with gram-negative organisms, lung abscess, and occasional septicemia," according to Dr. Thomas L. Petty, Associate Professor of Medicine and head of the division of Pulmonary Diseases at the University of Colorado Medical Center. He and Dr. David G. Ashbaugh were the first to describe ARDS in 1967 as an identifiable respiratory emergency with a uniform clinical picture.

"It's important to recognize that there are all kinds of ways to injure the lung, and ARDS can result from a variety of machanisms," Dr. Petty says. "It's not a new syndrome – it's been around for a long time – but it's a desirable lumping together of all pulmonary injuries that lead to the same kind of clinical picture. This also provides a framework on which to establish systematic therapy."




Dr. Blaisdell

Dr. Petty

Patient with AROS due to massive aspiration and smoke inhalation. Chest x-rays and simultaneous factors of oxygen therapy (liters by mask figure 1 and measured inspired oxygen tensions of tracheal air PIO2) compared with simultaneous arterial oxygen tensions (PaO2). Figure 1 was taken on admission to emergency room, and figure 2 was taken six hours later with patient on volume ventilator and 10 cm. PEEP. In figure 3 40 hours later, note x-ray clearing but persistent oxygen transport abnormality. Patient is off respirator and recovering in figure 4. Normal PIO2 for Denver is 118-123 (barometer 617-637 mm. Hg). The inspired to arterial tension difference is a useful clinical index of impairment to pulmonary oxygen transport.

"Fatalities are usually a result of septic complications, including pneumonia, with gram-negative organisms, lung abscess, and occasional septicemia."

dine, an anti-influenza virus agent, might prevent the onset of influenza that may lead to ARDS. Further, in patients who already have a massive viral pneumonia, he advises the use of diuretics and limited fluid intake, to avoid leakage of fluid into the lungs that might aggravate the patient's condition and precipitate ARDS.

No matter what the causes, about which there is considerable disagreement, ARDS presents a distinct clinical syndrome. Patients suddenly develop marked tachypnea, dyspnea, and cyanosis due to a progressive fall in arterial oxygen tension.

The lungs typically are dry to auscultation and tracheobronchial secretions are minimal. A chest x-ray reveals the progressive development of infiltrates, initially reticular, which may progress to complete consolidation, bilaterally.

"The infiltrates develop slowly and disappear slowly as opposed to classic pulmonary edema, with which this syndrome is often confused," says Dr. F. William Blaisdell, Professor of Surgery at the University of California School of Medicine, who has considerable experience in treating the ARDS.

"Respiratory function studies reveal evidence of arteriovenous shunting, decreased compliance, and decrease in effective lung volume. Unless therapy is vigorous and properly applied, death may occur in 48 to 72 hours," he stresses.

Pathophysiologic changes

Physicians agree that basic changes take place in the microvascular structure of the lung. "Initially the evidence suggests that the changes ars due to an abnormal increase in vascular permeability," notes Dr. Blaisdell. "This is gross enough to permit the loss of protein and red blood cells into the interstitial space and then subsequently into the alveoli."

The accumulation of interstitial fluid interferes with surfactant activity and leads to poor effective compliance or stiffening of the lungs. As a re-

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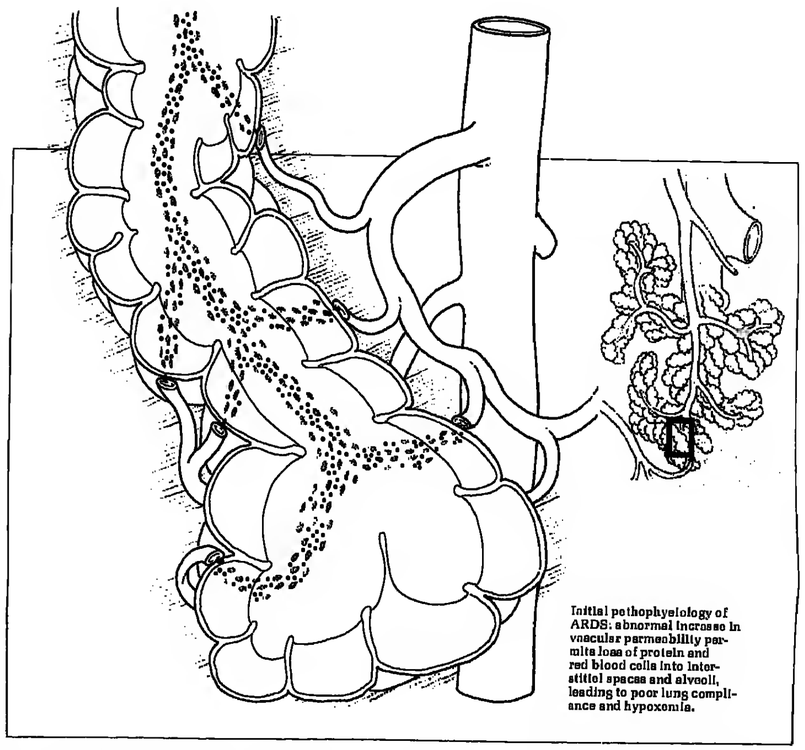


Initial pathophysiology of ARDS: abnormal increase in vascular permeability permits loss of protein and red blood cells into interstitial spaces and alveoli, leading to poor lung compliance and hypoxemia.

ARDS

continued from page 17

sult, the lungs are more reaistant to inflation and the work required to inspire is increased, perceived by the patient as dyspnea and resulting in hyperventilation and an initially low pCO_2.

Second, a atiff lung decreases the volume of air remaining in the lung after expiration by pulling harder against the chest wall than a normally compliant lung. Some areas of the lung collapse, and blood passing auch nonventilated areas cannot become oxygenated, even when the patient is breathing 100 per cent oxygen. The result is hypoxemia, measured as low arterial oxygen tension.

In order to raise arterial oxygen levels respiratory support with mechanical ventilstors is standard. However, both Dr. Petty and Dr. Blaisdell agree that in order to reduce the incidence of superimposed infection, oral or nasal intubation is initially prefarable to a tracheostomy, unless reapiratory support is needed for more than three or four daya.

"I believe thst attention towards avoiding contamination of the airway in these critically ill patients has, at least in our environment, cut the incidence of superimposed infection," notes Dr. Blaisdell. "Measures such as avoiding early tracheostomy, the use of sterile gloves

"We feel very strongly that prophylactic antibiotics are harmful and of no use at all."

and sterile aspirating tubes which are discarded after one use, and the careful sterilization of all tubing and ventilator equipment between patients and from day to day on any given patient are important to avoid contamination."

Over the past few years the mortality for ARDS haa been lowered from 70 per cent to less than 20 per cent at San Francisco General Hospital, where Dr. Blaisdell is chief of surgery.

Antibiotica contraindicated

The use of prophylactic antibiotics against infection is felt to be contraindicated by both physicians.

"We feel very strongly that prophylactic antibiotics are harmful and of no use at all," Dr. Petty stresses. "In a recent paper we showed that infection was most likely to occur in patients who had the most prophylactic antibiotics, and there was no evidence at all that they prevented sepsis."

Dr. Blaisdell concura, noting that at San Francisco General thay do not uae prophylactic antibiotics because patients become much more susceptible to superinfections.

"We believe that cultures of the secretions from the tracheobronchial tree should be taken daily in a critically ill patient to permit identification of the infections as they occur and point tha way to specific treatment, based on sensitivity."

Depending on the nature of the organism responsible, Dr. Blaisdell feels that penicillin, in high doses, is the preferred antibiotic against mouth infections; gentamycin, cephaloaporin, and kanamycin each may he of value againat specific gram-negative organisms. "We try to use the most appropriate specific action antibiotic," he notes.

Dr. Petty points out that "one rarely encountera gram-positive bacteria as a complication of ARDS, and I would say it is extremely rare as a cause." Thua, he, too, finds gentamycin and kanamycin the two most uaeful antibiotica to combat gram-negative bacilli. He also notas that "attempts at isolation of thesa patienta are of little value, since the organisms causing pulmonary infection are almost always of endogsnous origin, from another infected site."

Oxygen toxicity

Oxygen toxicity, cauaed by prolonged administration of high concentrations of oxygen, is another avenue by which pulmonary damage and infection occur, aince high oxygen levels interfere with lung antibacterial defenses and can, by themselves, cause ARDS.

High concentration of oxygen at the alveolar level is apparently toxic to pneumocytes, and hence to surfactant production, and results in interstitial hemorrhage and edema similar to that occurring in ARDS.

Ideally the patient ahould receive the loweat possible oxygen content needed to maintain the arterial oxygen tension (pO_2) between 60 and 80 mm. Hg according to Dr. Blaisdell, and in order to maintain proper oxygenation, constant monitoring of arterial blood tension is now routine in intensive care units.

"If oxygen fractiona of more than 40 per cent are required for longer than a few days, we would use positive end expiratory pressure (PEEP), which usually allowa you to use a lower percentage of oxygen," Dr. Petty notea. "You may have to use 100 per cent oxygen initially, but for more than 24 hours this is very dangerous."

"Respiratory function studies reveal evidence of arteriovenous shunting, decreased compliance, and decrease in effective lung volume. Unless therapy is vigorous and properly applied, death may occur in 48 to 72 hours."

Steroids controversial

The use of staroids in ARDS therapy is controversial, at best. "Theoretically," Dr. Perry explains, "they are valuable in preventing white cell aggregation in the lungs and in promoting the production of aurfactant. They effectively combat the action of fatty acids in the lungs, and they atabilize cellular membranea."

In addition, steroids may minimize interatitial edema. Dr. Petty feels that, particularly in trauma, and possibly in viral infections, steroids are useful for two to three days at most. However, in a paper presented at a sympoaium on respiratory failure at Richmond, Va., he noted: "Clinical experience indicates the use of corticosteroid drugs is highly beneficial in patienta with the adult respiratory distress syndrome."

Dr. Blaisdell totally disagrees, feeling that the danger of lowering body immunity with steroids far outweighs any possible benefits derived. "I'm not convinced that steroids have done anything to lower mortality. They clearly knock out the immune mechanisms, and infection is often the final common pathway of damaged lungs."

He feels that the rationale for steroids is based on the assumption that, if given before clinical insult, they can decrease the damage demonstrated by stabilizing cells and cell membranes, rendering them leas vulnerable to shock damage.

He further points out that the favorable action of corticoids may be due to an effect in modifying the coagulation mechanism but that heparin is much more effective for this purpose. However, since intravaacular coagulation, or sludging, within the pulmonary capillaries is only conjectural, and because many cases of ARDS are complicated by acute gastrointestinal hemorrhage, many physicians believe heparin should be administered with caution, if at all. □

Most ARDS patients require respiratory support with a machanical ventilator

epiglottitis

continued from page 15

and noted to be erythematous but not swollen in four. The epiglottis was not visualized at all in the three patients with epiglottitis."

However, x-ray examination confirmed diagnosis in these three patients and indicated subglottic narrowing in 16 others.

The key criteria in x-ray examination appear to be the speed and efficiency of the radiology department and the degree of respiratory distress of the patient.

"If you have time, x-rays are fine, and we do them if it's possible," notes Dr. Baxter, "but

Direct visualization, by depressing the tongue, may have catastrophic consequences by precipitating obstruction.

the majority of children arrive in pretty severe straits, and they cannot tolerate being moved to an x-ray department, so we take them right up to the operating room to establish an airway."

Dr. Baxter feels that a pediatrician without access to the expertise of an otolaryngologist or anesthesiologist, if he is capable of passing an intratracheal tube through a distorted and intensely inflamed area, should intubate the child and then get him immediately to a center where there are facilities. Cases have been reported of tubes' slipping out during an ambulance ride and the child's dying.

Nasotracheal intubation, rather than tracheotomy, has baen tried with considerable success in Scandinavia, but Dr. Hawkins feals that, in addition to possibly slipping out, they may cause irritation and possible laryngeal stenosia once they have been removed. "A nasotracheal tube is less well tolerated, it's uncomfortable, and the patient has difficulty esting with it," he says.

Routine tracheotomy

Routine tracheotomy is another area of considerable controversy. Most physicians who have loat a patient feel that the dangers of trachaotomy and the small scar it leaves are minimal compared with the inability to establish an emergency airway should obstruction occur rapidly.

"I'm not in favor of conservative management," notes Dr. Hawkins — "that is, avoiding doing a tracheotomy. Some feel that if the child looks as if he will not get into serious airway distress, then you should manage conservatively, but it's a very rapid progression.

"From outward appearances a child may look as if he is doing very well and then suddenly close off. There are numerous reports of this happening, and my feeling is that you can't be sure how they are going to do. So that unless there are contraindications, all children should have a tracheotomy."

His usual procedure is to establish an airway by slipping in a bronchoscope and then proceeding with a tracheotomy nt

"Better to have a live child with a smnll scnr on his neck than an unscnrred child lying in his coffin."

the level of the third and fourth tracheal rings under local or general anesthesia, depending on the location of the patient and the availability of an operatingroom.

Dangerin tracheotomy

"There is great danger in doing a tracheotomy in a struggling child," he admits. "You may cut some of the vital structures in the neck or the pleurs, which mny balloon into the wound. The patient may suck air through the wound into the mediastinum. The problem is much alleviated when you have established an airway, since many children will then just go to sleep."

"Better to have a live child with a small scar on his neck than an unscarred child lying in his coffin" is the feeling of Dr. Baxter. In his management of 103 children with epiglottitis, 100 received routine tracheotomies at the time of diagnosis. One child died on his way to the operating room for a tracheotomy.

"In children we have always done a routine tracheotomy," he saya, "because epiglottitis is a treacherous condition which can lead to obstruction very rapidly. There is aome tendency to put children on steroids and watch them, but someone experienced in intubation should be there constantly in case the child goes into respiratory arrest." Generally he feels that medical management alone is neither wise nor prscticnl.

Steroids not reliable answer

Dr. Hawkins also warns against relying on the anti-inflammatory effects of steroids. "It would be dangerous to rely on steroids to slow progression of the swelling, because epiglottitis is such a deceptive condition that you may think it is working and the patient may become obstructed just a few minutes later."

Adults often do not need tracheotomies, he has found, since the airway is much larger, and what would cause obstruction in a child may cause only huskiness in an adult. "Only four out of 17 patients reported in our study needed tracheotomies, and in five patients since then we have not done one," he says.

Dr. David Smith, of St. Christopher's Hospital for Children in Philadelphia, sgrees that "doinga tracheotomy ia a much smaller risk than sitting on a patient with acute epiglottitia without skilled hospital staff in constant attendance. Given a patient whose distress is mild, however, we are willing to temporize handling him medically with antibiotica, humidity, and corticosteroids under continuous monitoring. There is great dependence on the lateral neck radiograph in our hoapital and there is no manipulation of the patient if the diagnosia is confirmed by this study."

Once an airway has been established, intravenous ampicillin is the antibiotic of choice to combat H. influenzae type B and is also effective againat a broad spectrum of bacteria responsible for epiglottitis in adults. A cold-mist tent and sometimes steroids are useful in combating edema.

Usually swelling subsides within two or three days, and the tracheostomy can be removed without difficulty within a week.

"High index of suspicion"

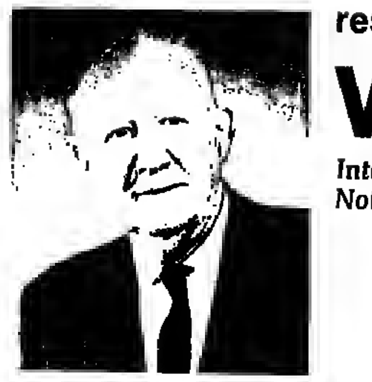
There is no known preventive medical treatment for acute epiglottitis, but a "high

"In children we have always done a routine tracheotomy because epiglottitis is a treacherous condition which can lead to obstruction very rapidly."

index of suspicion in a patient with a recent onset of sore throat and dysphagia will help rule out the disease," according to both Dr. Hawkins and Dr. Baxter.

"Looking in at the throat in acute, painful dyaphagia will often not be enough. You may have epiglottitis along with a red pharynx, and the physician may think the patient only has pharyngitis," warns Dr. Hawkins. "If, however, you look in and see the pharynx is not red, then you really should suapect epiglottitis and do everything to confirm or rule out that diagnosis."

Increasing awareness on the part of pediatricians is helping to lower death rates. Now that adults also appear to be more susceptible to H. influenzae infection, internists and family prsctitioners should also become more knowledgeable about the diagnosis and treatment of acute epiglottitis. □



respiratory disease perspective:

where we're going

Interview with Dr. John R. Seal, *scientific director, Notionol Institute of Allargy & Infectious Diseoees.*

Where is NIAID going in its research with respiratory diseases?

We have many unsolved problema. Viruses are certainly the major problem for the over-all population, with respiratory disease a tremendous nuissnce and a real drain on the medical profeasion. I think, however, we can devalop vaccines against a majority of these.

I expect more new viruses to be isolated and identified within the next five to 10 years.

I am also confident that we will increase our capabilities and efficacy with antivirals, be it interferon or something else.

While there is no panacea for the common cold, I believe the ultimate answer is an effective chemotherapeutic prophylactic or treatment rather than a vaccine.

As our understanding of the immune system increases, as capabilities to control the immune reaction and specifically manipulate it grow, we should certainly be able to make progress with organ and bone marrow transplants.

What we need now is new methodology and naw technology for solving many current problems.

Allergy has moved from a situation in which, a decade or so ago, it might have been considered almost a form of witchcraft. Now it is a very respectable science, based on solid acientific information that is increasing every day. We expect tremendous progress in the allergy field in the next 10 years or so.

What allergy research is being concentrated on?

Allergy is a field that has really begun to explode. We hava a better understanding of the hyperaensitivity expressed in man in such diseases as hay fever, aathma, and the delayed hypersenaitivity related to cellular immunity. NIAID has created 17 Asthma and Allergic Disease Centers to try to move the immunologic advances into the clinical setting for the improvement of diagnosis and treatment.

The total expenditures last year for 13 centers and reagents was about $1,800,000. We are trying to make reagents to ragweed pollen and make these available to scientists interested in desensitizing patients against hay fever specifically or for use in other diagnostic tests for allergy to ragweed and to the components of pollen rather than the whole pollen. We are supporting the allergy center directors to gather here at NIAID annually to discuss common problems and how to solve them.

Would you please describe your vaccine development program?

We are currently working on influenza, respiratory syncytial virus, and parainfluenza vaccines. Field trials of pneumococcus vaccines are being held in North Carolina and California. We will have enough evidence in two to three years on the pneumococcus vaccine to determine its efficacy, but it does look promising at this time, offering hope for licensing the vaccine in the future.

In addition, the National Institute of Child Health and Human Development has a field trisl under way with H. influenzae type b vaccine. The effort to develop this vaccine is a significant newadvance within the last five years.

We are also conducting experiments with streptococcus and mycoplasma vaccines.

There is a continuing effort to develop live attenuated RSV vaccine for children. This is necessarily slow due to problems of getting stable attenuated viruses made and tested in the laboratory, ensuring their stability, and identifying markers of attenuation before clinical experimentation on humans. With difficulty of finding older children or adults who are nonimmune, the going is very slow. We simply must find the correct balsnce to avoid symptoms yet retain enough infectivity of the virus to stimulate immunity.

"Viruses are certainly the major problem for the over-all population, with respiratory diseases a tremendous nuisance and a real drain on the medical profession."

What is the current status of interferon, its problems, and potential?

We still do not know the full potential of interferon for protection against human viral disease. In an experimental procedure last year, it was shown that exogenous interferon applied to the nasal mucoss prevented transmission of rhinoviruses and infections in human volunteers.

A major problem is finding an effective interferon inducer. Investigators concentrated on an artificial inducer—poly I:poly C—that has fair potency in some animals. Man, however, has a nuclease, a blood enzyme which breaks down poly I:poly C very rapidly, preventing the possibility of real stimulation. In addition, poly I:poly C was somewhat toxic in man. The assumption underlying thia research was that with severe and life-threatening viral infections you can accept more toxicity and riak than with the common cold.

Since we could not solve the nuclease problem, however, most work on poly I:poly C has been dropped. We are looking for other biologic inducers, such as extracts from some of the gram-negative organism fractions that have been found to induce interferon.

However, there is still an effort to find a more stabilized and effective poly I:poly C, and there may be preliminary testing of a modified form of poly I:poly C later thia year by the National Cancer Institute. Their researchers see potential of interferon inducers for ameliorating some types of cancer. We believe that the greatest use of an interferon inducer will be in the treatment of severe viral infections, such as disseminated vaccinia or herpas encephalitis.

"...producing and obtaining sufficient quantities of interferon is our biggest manufacturing problam."

Another problem is that only exogenous interferon is available for use now. Interferon is fairly apecies-specific. It is basically grown from human tissue culture, and this requires many, many cells to make large quantities. This is a difficult and expensive procedure.

In the studies on preventing the common cold, some 14,000,000 units of interfaron were used for each individual, and the cost was about $2,000 per person. This emphasizes the fact that producing and obtaining sufficient quantities of interferon is our biggest manufacturing problem. I don't know how far we can go as yet in enhancing the amount of

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where we're going

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interferon that can be gotten from a tissue culture.

There is yet another problem with interferon inducers. After an individual has been treated with an interferon inducer, he becomes refractory to further stimulation. It takes about a week for an individual to overcome this, so he can only be stimulated about once a week. In the meantime, his level has been stimulated, and then it drops back almost to the base line. He has what appears to be an unprotected period after induction before he can receive another shot to get a response.

We are also investigating interferon's potential role in fighting rabies. There is fairly good experimental evidence

"...the research we consider most promising is the better understanding of the role of the various components of immunity in these viral infections."

that the combination of vaccine and interferon inducer or exogenous interferon is more effective than the vaccine alone. We should know much more within two to three years. What we need now is a cooperative clinical study between a number of centers, hospitals, and research institutions, using a common protocol. This is an expensive undertaking in terms of time, people, and money, but we are working toward this goal.

What work are you doing against influenza?

Influenza is really the major problem in viral respiratory diseases. In the last five years a tremendous amount of information has been gathered on the influenza virus, its behavior in annual appearances, and major genetic shifts every 10 years or so, causing global epidemics.

Regarding control of influenza, I think the classical inactivated vaccines have been vastly improved and purified.

What led to this increase in purity and reliability?

Our advancing laboratory technology was a primary factor. Development of the zonal centrifuge enabled us to handle large volumes of fluid in continuous high-speed centrifugation. More impurities that derive from the eggs on which the virus is grown can be removed with zonal centrifugation. Other techniques were developed that "cleaned up" the virus and that eliminated egg components and other impurities causing adverse reactions.

Observation on recombination of influenza virus strains is another factor in manufacturing vaccines of high potency and purity. Several years ago, one investigator found that by recombining a new strain of the virus with an older laboratory strain that grows well in eggs, he could impart the growth capability to the new strain. It then grows out to a much higher titer. This method has been refined in recent years and is generally used now in vaccine manufacturing.

What is being learned about local immunity?

Some years ago, studies showed that parenterally administered influenza or rhinovirus vaccine does not stimulate any immunity in the upper respiratory tract, whereas locally administered vaccines, both live and inactivated, do create an immunity.

The whole concept of live attenuated influenza vaccine is based on the idea that immunity created through a harmless infection of the respiratory tract is superior to other methods because local antibodies will be formed, and cells which form them will be sensitized. The invading virus will tend to be cut off at the site of implantation before having a chance to grow and do much damage. Circulating antibodies do not reach the site until the damage is done and an inflammatory response occurs.

An interesting approach to local immunity involves temperature-sensitive (ts) mutants of viruses. The virus is limited in its growth characteristics by temperature, so that it will not grow, for example, over a temperature of 39°C. When the vaccine is locally administered in the nasopharynx, the virus cannot descend and replicate in the lungs because the temperature is too high. An experimental vaccine using the ts-1-E mutant virus prepared this way was placed in human subjects. In those persons with an upper respiratory tract infection there were no symptoms in the lower respiratory tract, and these people were solidly protected when challenged later with wild-type viruses.

In another approach, investigators have worked with the cold-adapted viruses. They exposed and grew the virus under

"While there is no panacea for the common cold, I believe the ultimate answer is an effective chemotherapeutic prophylactic or treatment rather than a vaccine."

cold conditions and then picked the clones that grow best under lower incubator temperatures. Their concept is basically the same, though, as the virus is restricted in growth at temperatures in the lungs but grows well in the upper respiratory tract. Almost any change in these viruses does decrease their capacity to cause clinical illness.

Would you please describe the institute's work with coronaviruses?

This family of viruses is clearly related to outbreaks of common colds during the midwinter season, as established by epidemiologic studies within the last two or three years, although the virus had been isolated a decade ago.

Coronaviruses are very difficult to grow, and they must be grown in human organ culture. Three serotypes in this family have now been identified, and we are now attempting to identify and characterize other common cold viruses in order to show their importance in respiratory disease.

How is research funding divided among the areas you've discussed?

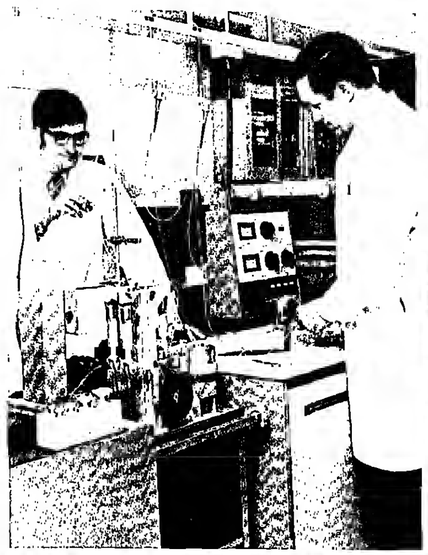
Last year we spent about $1,200,000 on influenza, and we expect this to reach $1,800,000 in 1974. For other respiratory virus infections we spent about $1,500,000, and this figure will probably show a slight increase. We also spent roughly $2,800,000 for antiviral research last year, and in 1974 we expect to spend the same.

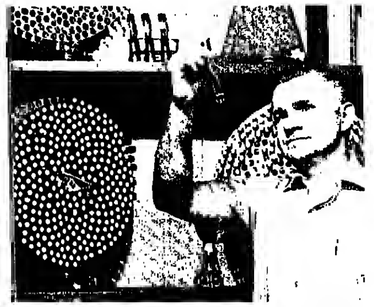
What is the most promising research being undertaken?

I think that in respiratory infectious diseases the research we consider most promising is the better understanding of the role of the various components of immunity in these viral infections. Also, our technology in the area of manipulating immunity is becoming more effective.

We have a far better understanding of viruses from our molecular biology work.

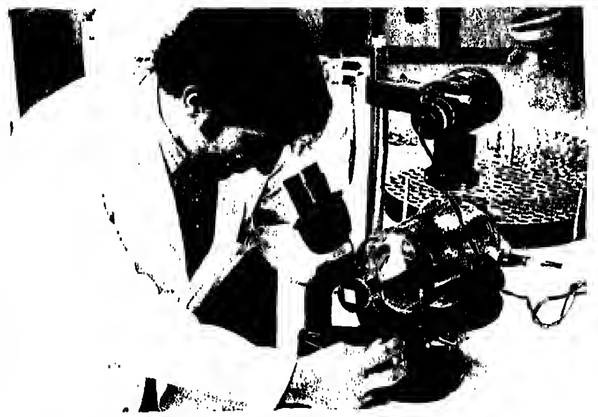
Research with live attenuated virus vaccines has great potential advantages. The quantities needed to immunize entire populations, and the eventual cost of such vaccines, should be far less than with inactivated vaccines and far more effective because they promote a natural immunity rather than an artificial immunity to the virus. □



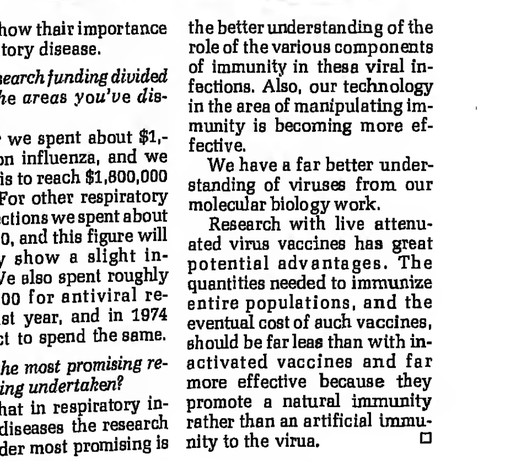


NIAID Vaccine Development Program

Investigators prepare respiratory virus specimen for purification in zonal centrifuge.



Nasal washings from common cold sufferers are prepared in different cultures, placed on rotating roller drums, and incubated in this "hot room" at 33° C.



Scientist looks for cytopathic effect in a viral culture that might serve as a live vaccine for inoculation in human volunteers.

how I treat bronchiolitis

Dr. Ira Lawrence Hemminga, *pediatrician, Lexington Clinic, Lexington, Ky.*

I FREQUENTLY WILL SEE bronchiolitis patients in groups of five or six. From winter into spring is the season for this illness. I've seen three cases in the last week.

A bronchiolitis patient will present with some wheezing, associated with rapid respiration, shortness of breath, coughing, and will usually have the appearance of a mild upper respiratory infection involving the nosa and throat. I usually use an x-ray in my diagnosis and find hyperaeration without any infiltrates or signs of pneumonia.

I don't think you can distinguish between bronchiolitis and asthmo in some patients, particularly the very young. I frcquently give them apinephrine and see how they reapond. If this helps, it leads you to think that the problem is more asthmatic, although that's not always true.

I always watch bronchiolitis patients afterwards to sea if they do develop asthma. If they have what you would diagnose as bronchiolitis two or three times, then I think it's probably asthma developing.

You must always watch out for foreign bodies when making a diagnosis, not only by studying ths x-ray but also by watching to aee if there'a any change that might suggest a foreign body.

I treat most bronchiolitis with vapor and fluids and put some patients on some sympathomimetic medication, usually ephedrine with expectorants. I try to treat them at home unless they become so short of breath that it's worrisome. I find I csn treat about half of the cases at home.

In the hospital, I put the infant in a croup tent, with intravenous fluids, and I take a culture to identify pathogens. Usually no pathogens are identified in bacterial culture, but occasionally I'll find streptococcus and treat with penicillin. But it is rsre to find bacterial infection. Steroids have been of no benefit.

Most of the time I use compressed oir to blow the vapor into the tent rather than placing the child in oxygen, but if arterial pO_2 is low, then we would use oxygen.

Fluids

I encourage infants to take fluids by mouth if they will, but some get so short of breath thot they're unable to eat well or take fluids well, or they may start to vomit. Then it's necessary to go to intravenous fluids. A high-fluid diet ia necassory becauae there's a tendency to dehydration. Whan you're breothing aa rapidly as they do, you blow off body fluids. There's some moisture you lose just from rapid breathing, and you need to replace this. Also, you're trying to keep the mucus as thin as possible. And the more fluid they take in, the thinner the mucus is.

When the child ia sent home from the hospital, I tell the parents to keep them hydrsted and watch them for further signs of respiratory distress, although it is unusual for pure bronchiolitis to recur. □

Dr. Richard T. Cushing, *pediatric allergist, St. Louis Park, Minneapolis*

BRONCHIOLITIS is difficult to differentiate from bronchial asthma in the small infant. Since it is difficult to distinguish bronchiolar disease from small bronchial obstruction, the pediatrician may be able to make the proper diagnosis only in retrospect.

Certain clinical features, however, should suggest the etiology as infectious instead of allergic. These features include the age of the infant, family history, type of onset, and the response to epinephrine.

Bronchiolitis primarily affects infants from under six months to one and one-half years. There are usually signs of an acute upper respiratory infection preceding a gradual onset of wheezing dyspnea, which may rapidly progress over a few hours to tachypneo and alarming air hunger. Fever is usually low-grade.

Besides intercostal retractions, fine wheezes are heard bilaterally and may occur in both the inspiratory and expiratory phases of the respiratory cycle. Asthmatic wheezes tend to be more expiratory. Clearing of wheezing after a small dose of epinephrine (0.05 ml. of 1:1,000 aqueous epinephrine) repeated in 20 minutes may ba a useful, though not invariabla, sign of asthmatic breathing.

Chest x-raya usually show hyperinflation of the lung fields without much infiltrate, but atelectasis may be present. Films should always be taken as part of the evaluation.

The hemogrom is rarely helpful, and bacterial cultures usually show normal flora, since the respiratory syncytial virus has most often been associsted with the bronchiolitis syndrome. Ordinarily, the trestment of bronchiolitis should not be attempted out of hospital because of the crucial supportive meosures required for the ocute phase of the illness. These supportive measures inclnde humidified oxygen and intravenous fluid therapy to combot hypoxemia and dehydration.

Basic treatment is olmost entirely supportive. Bronchodilators, such as aminophylline (4 mg. per Kg. every six hours), are indicated only if test doses seem to provide improved air exchange.

Antibiotics are ineffective for treatment, but toxicity of the infant and caroful clinical judgment may dictate their use. If so, I would chaosc ampicillin 100 mg. por Kg. per 24 hours in four dividad dasas. Most studios show no clear benefit from corticosteroids.

Rccovery phosc

Right heart-failure must be watched for, progressive liver enlorgement being an important sign. Digitalization would then be indicated.

In the recovery phase expectoranta, such aa SSKI, 2 or 3 drops three times a day, msy help liquefy the copioua secretiona and introbronchiolar debris.

In my experience, bronchiolitis rarely recurs, and if wheezing is recurrent, asthma is more likely as a diagnosis. In fact, researchers have shown that hslf of those infants who have bronchiolitis will eventually become asthmatics. Whether thia is a causal relationship or represents a predisposition of the infant to develop obstructive airway disease is not known. □

Dr. William Berenberg, *chief, Inpatient Service, Boston Children's Hospitol, Boston.*

THERE HAVE BEEN epidemic proportions of bronchiolitis in the Boston area during the last few years in both late spring and winter. But it's not only seasonal. When you get an outbraak of viral disease in the community, it can coma at any time.

Bronchiolitis can be difficult to distinguish from aathma. I diagnose it mostly on the basis of age, fever, acute onset, failure to respond to asthmatic therapy, and appearauce of x-rays. Usually, there's no great problem. If you have a child who's been well, who's under a year of age, then gets a respiratory infection — cough, fevar, wheezing, and respiratory difficulty — that sets it spart from nsthma on the basis of age, fever, and nature of onset. It's a lot more difficult to tell from infectious asthma. That can start the same way but usunlly is seen in an older ogegroup.

I usually usc an x-ray, because thu cases of bronchiolitis that I see are scvere. For more mild attocks, you don't need an x-roy. I routinely do a culture to make sure the infection is not bacterial and to make sure there aren't any secondary bacterial invaders.

I seldom use epinephrine in treatment because it doesn't do very much good. I occasionally use it as a test to see if they do respond. If I get a dramatic response, I'm apt to feel it's not bronchiolitia. It makes me think there's an asthmatic component. I use a bronchodilator whenever I think there is sufficient bronchial spasm to demand a trial but do not anticipate much effect from it.

Mild cases of bronchiolitis can be treated at home with a bronchodilator and cool mist. The parents con build a croup tent. As long as they use cool mist, it's all right, but hot mist should be avoided. I prescribe the same supportive measures you would use in treating any other viral infection, including a high-liquid diet.

In the hospital, I treat the child pretty much the same as in the home, using mist most often, giving oxygen only if he needs it and intravenous fluids only if he isn't taking fluids. You don't want to overfluid. I also use physical therapy in the hospital, pounding the chest in an appropriate fashion to prevent any plugging. Thot is usually done twice a day, occasionally three times.

Antibiotics

There's a great dispute over the use of antibiotics. It depends on how sick the child is and whether or not you want to wait for a culture to come back and whether you think there's secondary infection. With viral bronchiolitia, patients do not respond to antibiotics. At best, you may reduce the complication rate. What kind of antibiotic to use depends on the age of the child, the degree of illness, and frequently the selection is bosed on what's prevalent in the community at any one time. If in doubt, we tend to favor ampicillin, since H. influenzae infections may mimic bronchiolitis in the young. If you're deoling with an outbreak of mycoplosma you probably would use tetracycline or erythromycin.

There's considerable controversy over whether hydrocortisone has ony value in treating bronchiolitis. It's probably of no value or doubtful value. I use it only if I am dealing with a critical aituation — a desperately sick child who's going into shock. □

Stress Snapback Portends A Child's Later Breakdown

Continued from page 3

Indian Ocean island of Mauritius. With no attention to heredity or other possible screening factors, the fast autonomic nervous system recovery from stress will be studied as a possibly predictive signal for those at high risk of later mental breakdown.

A group characterized as "high-risk" has already been selected. Stress recovery measurements include skin conductance, skin potential, and electrocardiogram. Others, charncterized as "low-risk," have had medium recovery rates and medium amplitudes of respoose to low stress. From both groups, 200 children have been raodomly selected for placement in one of two special nursery schools for close observation or for follow-up in the community.

High-Risk Children Cry More

In preliminary findiogs, the high-risk, fast-recovery group has iocluded a mucb greater number of children who cry uncootrollably, or qnietly but contiauously, during testing under mild stress. "In our earlier, Copenhagen study we found that those who were similarly difficult in the test situation were promioently amoog the brenk-down group," Dr. Schulsinger said.

The theoretical bnsis for the study, Dr. Schulsinger explained, dcrives from evidence that heredity is the best-established risk factor in schizophrenia.

"Additionally we know that certain environmental risk factors must also be of great importance. In 1967, 20 of 207 genetically defined high-risk subjects had suffered from mental breakdowns of various kinds," incinding severe schizophrenia, delinquency, alcoholism, or manifest bizarre symptomatic behavior.

"We asked ourselves: 'What distinguished these children from 104 matched, nonbreakdown controls?' We observed that certain psychophysiologic varinbles discriminated very well, and the best discriminator was a fast recovery time from n mild stress to the autoaomic norvous system."

He added that "the breakdown group was characterized by faster latencies of response, poorer extinction of the condltioned galvanic skin response (GSR), and greater reactivity at higher response amplitudes. All of these variables, with the exception of poor extinction of GSR, were to a lesser degree characteristic of the total high-risk offspring" in the Copenhagen study.

The Mauritius study, sponsored by the World Health Organization and the Danish Government and now under way for nearly 18 months, is focusing on preventive experimentation. "One thing we know we can do preventivcly is to counteract scrious social cruptions and upcoming parental separation. We are considering a variety of behavior modification techniques, in order to help the [high-risk] children withdraw less from conflictual social situations," Dr. Schulsinger said. "Of course, there nre ethical considerations to take into acccount, and we hope to have WHO aod NIMH experts advise us of these."

Drs. Schulsinger and Mednick are from the Psykologisk Institut in Copenbagen.

Hemodialysis Unit Takes to the Road

The nation's first mobile hemodialysis unit has already logged more than 6,500 miles since November through sparsely populated northern Michigan, eliminating the need for patients to travel long distances to centers for treatment. The unit, manned by two technicians, can cleanse the blood of two patients in three hours, making it possible to treat up to four patients a day.

Demand for Sterilization In Netherlands Increases

Medical Tribune World Service

UTRECHT, THE NETHERLANDS—The demand for sterilization in the Netherlands is increasing so rapidly that physicians may soon have difficulty in keeping up with it.

A survey of a 700,000-member insurance group showed that sterilizations of men increased from 10 in 1969 to 573 in 1971 and 1,136 in 1972. Sterilizations of women also increased.

Continued from page 11

clusion that Dr. Sackler has the audacity to state is that a zero population growth will automatically be attained when all mankind has adequate jobs, housing, and health care. Because of Dr. Sackler's ignorance of the actual facts of today's matters, he does not realize that these goals are out of the question for two-thirds of the population mankind has already obtained. The good life has been obtained by the affluent third by the use of stored energy and resources. These are not only less available but are fast becoming unavailable to the poor two-thirds of mankind. These shortages are at this moment making the peoples of Africa and Asia and South America, who are already at starvation's door, subject to mass die-offs, because adequate food is not available.

Perhaps when the die-offs which have begun in North Africa these past two years and in Bangladesh are more widespread, Dr. Sackler may be forced to acquire more details of mankind's actual situation and see what the demographers, conservationists, and the World Health Organization has already grasped—that is, that this earth could possibly support 1 billion at the United States standard of living. It cannot adequately support 4 billion now resident upon it. Not only the quality of life must deteriorate but mass die-offs must occur if the sexy naked ape persists at his present growth rate to overpopulate the earth.

PETER S. PINTO, M.D.
Ridgecrest, Calif.

. . . *Keep Them Coming*

I can't resist the impulse to oppose recent opinions on welfare sterilization. We all know the limitations of the welfare system and some of the people who live under it. Most of us agree on the problems which should be solved. The *methods* of solving them form the basis for disagreement.

My argument is with the *means*; not the ends. With no malice toward the particular physicians, I would like to disagree with their proposed methods.

For many years we have been bombarded with the philosophy of eliminating problems by preventing or eliminating people. This is really a primitive idea but is enjoying renewed modern-day acceptance. Population hysteria, "the unwanted child," quality control, etc., are all really expressions of a growing antipeople mentality.

The underlying logic seems to be: Very Few People—Very Few Problems. People are our most valuable ecological natural resource. They are important and should be conserved and preserved. The problems of poverty, violence, pollution, welfarism, etc., will not be cured through prohibiting people (yes, even by coercion, as the doctors suggest.) Have we forgotten that people solve problems as well as cause them? Society must eliminate human problems, not human beings.

GEORGE N. PASTO, M.D.
Gresham, Ore.

Wine Talk & Questions

You welcomed comments and questions about wine, and my question is this: Is it not true that any kind of grape juice, the way it is manufactured in this day and time, will have a certain amount of alcoholic content in it? If not, at what point does the manufacture of grape juice and/or wine start containing some alcoholic content? I ask this question mainly from a religious viewpoint in that some people who partake of wine say that those who partake of grape juice are wrong and vice versa. My point is this, that those who partake of grape juice probably are partaking of minute quantities of alcohol whether they know it or not. On the other hand, those who criticize those who partake of wine probably are partaking some themselves in minute quantities.

CHARLES E. GRAHAM, M.D.
Richardson, Tex.

John Chambers Replies

Grape juice becomes wine through a process of fermentation which can be defined as the transformation of sugar into ethyl alcohol and carbon dioxide by the action of yeast. In the production of commercial grape juice, the pressed liquid is held at a temperature too low for fermentation until it can be sterilized (i.e., pasteurized). Therefore no alcohol is formed.

Interestingly enough, the wild yeast which forms on the grapes is almost never used nowadays in the production of wine. Instead the wild yeast is eliminated, and specially prepared culture of yeast is added to the juice to insure a controlled, high-quality fermentation. Although it is possible for fermentive action between wild yeast and grape to begin before harvest, this never happens in the production of grape juice, the grapes for which are harvested early rather than late. Consequently there is no alcohol, even in minute quantities, present in grape juice.

Office for the Retarded

Medical Tribune Report

WASHINGTON—HEW Secretary Caspar W. Weinberger has announced creation of a new office for the mentally retarded and handicapped under the Rehabilitation Act of 1973, to be headed by Wallace K. Babington, director of the Office of Mental Retardation Coordination of the Health, Education, and Welfare Department.

Hepatitis-B Is Transmitted by Human Bite

Continued from page 1

and the teacher, who happened to be in the lunch room, turned him face down in order to pull the food from his mouth and throat. In doing this, she suffered two small tooth punctures, for which she was given tetanus shots.

"We were watching her," Dr. MacQuarrie said, "but not expecting anything like this to happen. Then, to prove that it was not something else, we had to go in and do an extensive investigation, re-examining the history of the people in the school and that of the teacher herself—35 blood tests were done."

Dr. MacQuarrie noted that the teacher's private physician had taken her detailed history and, despite the fact that there was no precedent, had singled out the accidental bite as the mode of transmission.

Other possibilities for the transmission, such as previous blood transfusions or the eating of raw shellfish, were eliminated by Dr. MacQuarrie, as well as by the teacher's physician.

One Other Carrier Revealed

The blood tests revealed only one other carrier among the students and staff and their families, a 14-year-old retarded girl, with whom the teacher had no contact.

The next step toward confirming the role of the bite was to determine whether the hepatitis-B of the teacher was the same subtype as that of the boy, which meant that Dr. MacQuarrie needed blood taken from the now-well teacher before she had recovered, and it was at this point that luck played a role.

"I began searching for a blood she had had taken in October [1972], and I was looking in February and March [1973], so I searched the labs for a blood test that had been done by her doctor. As far as we know, the blood had been thrown out after it was tested."

The blood was found in a laboratory freezer in Los Angeles, where it had been kept past normal limits. Someone had forgotten to tidy up.

The type and subtype of the teacher matched those of the boy.

"I then collected saliva specimens from the boy to see if the thing could be transmitted simply by saliva," Dr. MacQuarrie said. "I knew from the literature that hepatitis-B can exist in the saliva of people who carry the antigen in their blood."

This was a problem. "This is a retarded child—you can't just tell him to gargle and spit."

Sterile water was trickled into the boy's mouth. When he held the water he was tickled by the nurse, causing him to laugh and dribble, and the saliva was caught.

"We took five specimens, and all five were positive," Dr. MacQuarrie said.

Was this conclusive? "It is about as close as you can get."

What does this mean for the spouse of a hepatitis-B carrier?

"This is a complete unknown. What has been observed is that in the family relationships of carriers there is a higher incidence of secondary spread among their spouses. The kinds of studies going on focus on the sexual transmission of the antigen. This had been suggested, never proven—it is 'associated with.'"

Dr. MacQuarrie suggested that the transmission must be caused "by something that man and wife do that parent and child would not do. It has been sugested that it is some type of close contact, like sexual contact, but, indeed, it may be due to the mixing of saliva in the kind of kissing that would go on between husband and wife that would not go on between parent and child."

Nylon Network Gives Drainage In Lymphedema

Continued from page 1

easy to carry out, four longitudinal, eight apical, and seven circular threads (No. 1 nylon) are inserted with specially designed needles after incision of the skin and then tied to each other in Paris knots at the points of intersection. In this way a network is provided, extending over the region corresponding to the localization of the edema, from the foot, past the ankle region, to the knee or groin.

After insertion of the threads, the ends are cut off and the incisions sutured. The patient can be discharged as early as five days after the operation. The sutures at the incision sites are removed after 12 days, the subcutaneous network remaining in situ.

Patients Given Corticosteroids

Since the formation of fibroblast cylinders along the inserted threads defeats the object of the operation, all patients are given corticosteroids. The dose of 16 mg. of triamcinolone a day, for a month or longer, is increased if the patient has a tendency to form hypertrophic scars.

A lymphogram is made before the operation to ascertain whether only the superficial or also the deep lymphatics are reduced or missing. If the deep lymphatics are still patent, additional threads are inserted below the aponeurosis. The lymph can then drain along the superficial network and through the deep lymphatics.

So far no rejection reaction to the threads has been observed.

Cost of Training Medical Student $12,650 Yearly

Medical Tribune Report

WASHINGTON—The results of an 18-month study of the average annual costs of educating a student to the M.D. degree and to the first professional degree in seven other health professions are reported by the Institute of Medicine.

The estimated averages are $12,650 annually per student in medical school, $8,950 in osteopathy, $9,050 in dentistry, $4,250 in optometry, $3,550 in pharmacy, $5,750 in podiatry, $7,500 in veterinary medicine, $2,500 in baccalaureate degree nursing, $3,300 in diploma nursing, and $1,650 in associate degree nursing.

The report goes to the Senate Committee on Labor and Public Welfare, the House Interstate and Foreign Commerce Committee, and the Secretary of Health, Education, and Welfare. The study was contracted by HEW to the Institute of Medicine in June, 1972, under provisions of the Comprehensive Health Manpower Act of 1971. That Act (Public Law 92-157) initiated a program of Federal support of health professional schools on the basis of their enrollment, a system known as capitation grants.

Three Questions Asked

To help determine how much money might be required in capitation grants, Congress requested the study to find out what the national average annual education cost per student is in the eight professions, how those costs can be ascertained on a regular basis, and how they might be used in setting capitation rates.

For purposes of Federal and other aid to the schools, the study recommends a cost basis of "net education expenditures," which is a lower figure for all the professional schools except associate degree nursing. The net is calculated by subtracting from education costs the income received from research and patient care considered essential to education.

Annual average "net education expenditures" are put at $9,700 per student in medical school, $7,000 in osteopathy, $7,400 in dentistry, $3,100 in optometry, $3,050 in pharmacy, $4,900 in podiatry, $5,550 in veterinary medicine, $2,450 in baccalaureate nursing, $1,500 in diploma nursing, and $1,650 in associate nursing.

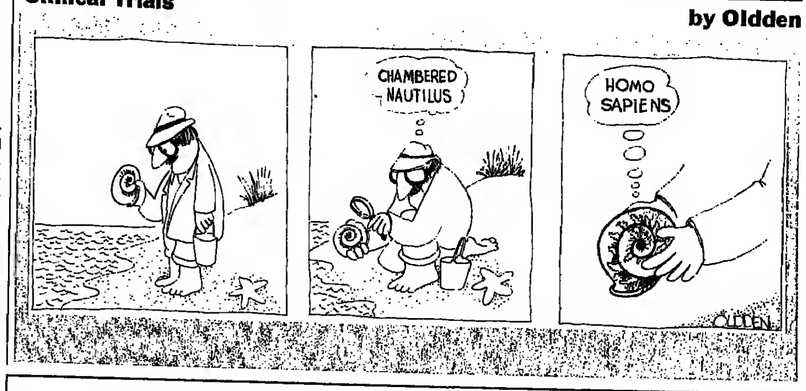
The study group's recommendations include an endorsement of Federal support for health professional schools as "a national resource," appropriation of capitation grants in such a manner as to make them a "dependable source of income" for the schools, a capitation formula that will maintain current enrollments rather than expand them, and grants based on numbers of graduates rather than numbers enrolled.

Vaccine Condemned

TOKYO—As a result of the detection of penicillin and tetracycline in manufacturers' samples, enough smallpox vaccine for 2,000,000 doses was ordered destroyed.

Clinical Trials

by Oldden



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Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema; minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

Lysosomotropic Therapy Aids in Leukemia

Medical Tribune World Service
From German Edition

SCHLOSS RAISENSAERG, WEST GERMANY—Lysosomotropic chemotherapy with DNA-daunorubicio complex has achieved remission in nine of 14 paticnts with acute granulocytic leukemia aod partiel remisaion in four others, it was reported here to the second Worksbop oo Activation of Macrophages.

Earlier, significant reduction of toxicity and iacrease of the therapeutic iadex against tumor cells had beeo obtained in aoimals by bonding daunorubicin or adriamycin to the vehicle DNA.

Dr. A. Trouet, of the Laboratory of Phyaiological Cbemistry, Louvain (Belgium) Catholic University, described the encouraging initial clinical results with DNA-daunorubicia complex.

If antineoplastic substaoces are bonded to a macromolecular vebicle that can be broken down by lysosomes, the result is known aa a lysosomotropic chemotherapeutic agent , he explained. It bas specific activity, directed only against cells with both a high mitosis rate and vigorous endocytosis activity, properties found in many tumor cells.

After it is admitted into the cell the vebicle is digested by lysosomes, and the chemotherapeutic agent is able to diffuse into the cytoplasm, the cell nucleus, and finally the extracellular space. Since most normal cells have low endocytosis activity, the toxicity for them of the lysosomotropic substance ought to be much lower than that of the free chemotherapeutic agent.

This lysosomotropic concepi was tested with daunorubicin (DNR) and adriamycin (ADM). DNA from calf's thymus or herring sperm was selected as the vehicle.

After bonding with DNA, both DNR and ADM lost their bacteriostatic activity. This was largely restored in vitro by incubation with lysosome extract and breakdown of the DNA.

Effectiveness Delayed in Vitro

In tests in vitro with tumor cells the effectiveness of the complexes was delayed but was just as great aa that of the free DNR or ADM. After intraperitoneal injection in mice, their toxicity was substantially less than that of the free substances.

Tbe therapeutic action of the DNA complexes was tested on DBA_2 mice with L1210 leukemia, Dr. Trouet related, and particularly interesting reaults were obtained with DNA-ADM. In low doses administered intravenously, tbia complex was at leasi as effective as free ADM. When tbc dosc was raised, the animals treated with free ADM soon died from tbc toxic effects. With tbc complex, however, about 60 per cent of the animals were cured.

Prelbminary trials with patients in the terminal stage of disease, Dr. Trouet said, showed tbnt the complex can also be administered to man without problems, though there was occasionally a significant hematologic reaction in cases that had previously been refractory to all chemotherapy.

DNA-daunorubicin was finally included in a combination therapy program for patients with freshly diagnosed acute granulocytic leukemia. The patients were first given 2 mg./sq. M. vincristine or 200 mg./sq. M. cytarabine, followed 24 hours later by two injections of DNA-daunarubicin (60 mg./sq. M.). This treatment was repeated several times, generally at one-week intervals.

It is not yet possible to assess the quality of the nine complete and four partial remissions, Dr. Trouet said, but he believes the high remission rate achieved with law toxicity justifies further therapeutic trials with larger groups, also using DNA-adriamycin.

Mouse Sperm United With Hamster Cell

Seeking to create a model system for studying how normal cells become malignant, investigators at Memorial Sloan-Kettering united five mouse sperm with hamster somatic cells in vitro, observing the transfer of genetic material from the embryo. Above, mouse sperm (A) can be seen as raised surface on hamster body cell it has just penetrated. Tail (B) remains outside cell, having crossed under tail of another sperm (C) that also burrowed in, but more deeply.

Low-Rise Hospital Better

Medical Tribune World Service

UTRECHT, THE NETHERLANDS—Low-rise bospital buildings are cheaper to build and operate, and lead to greater flexibility in long-term use, than high structures of the same bed capacity, according to a study by the architectural and technical commitiee of the National Hospital Institute here.

Propranolol May Mask Pain-Free Myocardial Depression

BY NATHAN HORWITZ
Medical Tribune Staff

HOUSTON, TEX.—Cornell cardiologists warn that the practice of stepping up propranolol dosage until the angina patient is pain-free may carry the risk of severely depressing the myocardium.

Propmnolol may mask the presence of "potentially severe myocardial depression . . . despite the absence of pain," said Dr. William H. Frishman, of New York Hospital–Cornell Medical Center, and he urged clinicians to compute dosage by "repeated" noninvasive assessment of the patient's left-ventricular function.

His recommendations stemmed from a controlled double-blind study of angina patients showing that "fatigue rather than pain" forced cessation of graded exercises in patients receiving incrementally higher doses of propranolol. Dr. Frishman spoke at a national conference on Coronary Artery Medicine and Surgery sponsored by the Texas Heart Institute and St. Luke's Episcopal and Texas Children's hospitals.

Oxygen Requirements Reduced

In detailing the study, Dr. Frishman noted that propranolol reduces myocardial oxygen requirements during exercise but has also been sbown to have a negative inotropic effect following acute intravenous or oral administration. "Our studies confirm these findings and extend them to measurements of left-ventricular function following chronic oral propranolol therapy."

The study series included 19 patients, all of whom had at least three angina attacks per week, a negative smoking history, and no evidence of valvular heart disease, hypertension, congestive heart-failure, or a recent myocardial infarction. Nine in the placebo group remained on the same regimen for six weeks; the 10 treated patients were started on 80 mg./day of propranolol for two weeks. Tho dosage was then increased to 160 mg./day in seven patients and to 320 mg./day in three.

The patients performed graded exercises on a bicycle ergometer und were monitored by phonocardiogram, electrocardiogram, and external carotid pulse tracings.

Serial exercise studies in the placebo group, Dr. Frishman said, showed no significant changes in work performance or heart rate–blood pressure product immediately after exercise. But in 10 patients receiving propranolol at 80 mg./day the mean total work load increased from 765 ±125 Kg./M. to 1,792 ±285 Kg./M. Improvement in work was associated with a significant drop in heart rate–blood pressure product from 16,800 ±1,535 to 12,000 ±885). When tbe propranolol dosage was doubled to 160 mg./day, the mean total work was 1,590 ±200 Kg./M. and the mean heart rate–blood pressure product was 12,1001 ±1,300.

"Neither of these values was significantly different from the data obtained with the lower dose. Hnwever, seven out of 10 patients on 160 mg./day did less work than on the lower dose, with fatigue rather than pain forcing cessation of exercise. In the remaining three patients, external work performed was greater at the higher dose, and they were therefnre increased to 320 mg./day of oral propranolol. At this higher dose all of the patients demonstrated a full-off in work performance, with fatigue being the end-point of exercise."

Work Appears to Be Limited

The findings at the higher doses were consistent with o decrease in left-ventricular function, "which appears to limit work at this point despite the reduction in oxygen consumption." There was no correlation of propranolol blood levels und improved work performance.

Dr. Frishman concluded that the most effective propranolol doses, at least under the study conditions, were 80-160 mg./day und that the lack of correlation between serum levels and clinical response dictates frequent noninvasive testing to determine optimal dosages for the individual angina patient.

Coauthors were Drs. Charles Smithen, Paul Kligfield, and Thomas Killip.

Difference Between Drunk and Diver Is In Their Sway

Medical Tribune World Service

STOCKHOLM—What is the differeoce between a drunk and a diver?

The drunk pitches while the diver rolls, J. Adolfson, of the Karolinska Institute, told the first Congress of the Undetsea Biomedical Society meeting here.

Disturbances of the upright position observed at 5 ATA with a CO_2 tension of 22 mm. Hg are similar to those of intoxication provoked by an alcoholemia of 1 Gm., Mr. Adolfsoo said, but the drunk oscillates mainly in the aagittal plane while the diver oscillates mainly in the lateral plane.

Swaying in divers, he said, increases with both hyperbaria and hypercapnia. At 5 ATA, it increases by 30 to 60 per cent with normocapnia and by 250 per cent with hypercapnia at 32 mm. Hg of CO_2. Swaying reaches 575 per cent of normal if the CO_2 level is increased to 44 mm. Hg.

IMMATERIA MEDICA

By DUDLEY STRAUS

The World Women Have to Inhabit

• A release from the United States International Transportation Exposition of 1972 (all right, things can get squirreled away on our desk!) reports: "Many exciting happenings. . . . Not the least of these will be the female fly-by by six members of the Ninety-Nines, World Association of Women Pilots. Led by Lorettu B. Foy in a 'skirted' Hughes helicopter. . . ." Skirted helicopter indeed!

• *"In the summer, the hardhats ate their lunches, sitting in the embrasures, dangling into ever increasing depths of space—20 feet, 40, 50, farther and farther above the ground—watching and whistling at the girls tittupping by on the street below. (So what's wrong with a sex image, whatever that is?)"* reports *Spectra* of the University of Miami School of Medicine. No comment, whatever that is.

• "A $110,000 negligence suit was filed in U.S. District Court Monday against a physician who allegedly treated a woman seven months for a pregnancy she said never existed," reports United Press International.

• Under the influence of the feminist movement, *Dental Images* of Marquette Dental School claims, the Marquette University Faculty Wives changed their name to Marquette University Women's Club, admitted all university-associated women, and published "Our Program—Towards Relevancy." The program, running from December to May, lists the following events: Champagne Noel, Children's Christmas Giving Party, Our Man From Washington, The Benefit—Tennis Everyone, a tour of the University of Chicago, Spring Splurge, Couples' Dinner Group ("La Grande Potluck"), and Family Picnic and Kite Fly-In. Men aren't the only enemy.

• By chance we came upon the definition of "virgin" in *Dorland* and then checked with *Blakiston* and *Stedman*. The product of our research:

Darland: "A woman or girl who has not had sexual intercourse."

Blakiston: "A female who has never experienced sexual intercourse as normally understood."

Stedman admits mules to the club.

* * *

The world gets odder and odder. We bought a box of finishing nails at the local hardware store and when we got it home discovered that it bore the following legend:

"Borneo Sumatra Truding Co., Inc.
Rutherford, N. Jersey
Made in Poland."

* * *

Advertising Age informs us that Mary Quant is putting out a line of cosmetics, designed for men and women, that includes a nail polish color named Evil Emerald.

Knee X-Ray Studies in Young Can Avert Needless Surgery

Medical Tribune World Service

MONTREAL—The adolescent athlete—particularly if his game is football—is at risk of epiphyseal injury to his knee from forces that would result only in ligamentous injury to an adult player, according to a team of physicians from the University of Texas Medical School at Houston.

Since "a ligament tear requires immediate surgery, whereas an undisplaced epiphyseal separation is successfully treated by casting alone," a mistaken diagnosis can lead to unnecessary surgery, an error avoidable by means of appropriate roentgenography, they told the 74th annual meeting of the American Roentgen Ray Society here.

Valgus Stress Chief Cause

In both injuries, the chief cause is a valgus stress to the lateral surface of the knee, most commonly the result of a "clipping" injury in football when the player, with his foot firmly planted, is blocked or tackled from the side.

In the adult, such a stress would lead to a rupture of the medial collateral ligament; in the adolescent, the same ligament transmits the stress to the distal femoral epiphysis or, less frequently, to the proximal tibial epiphysis, with resultant separation, the report noted. Most epiphyseal separations are roentgenographically and clinically apparent, it said, with the exception of a small number of undisplaced separations.

Physicians were urged to be alert to the possibility of epiphyseal injury in an adolescent when their first suspicion is ligamentous injury to the knee, particularly when a valgus force was sustained. Oblique and notch views should be obtained if standard projections are unrevealing, it was recommended.

The investigators were Drs. Lee F. Rogers, Geral Dietz, William Veatch, A. Ross Davis, and Stanley Jones.